REPORT TO THE WORKERS' COMPENSATION BOARD ON THE HEALTHY WORKER EFFECT

89-00516/

The Industrial Disease Standards Panel is a Schedule 1 Agency of the Government of Ontario attached to the Ministry of Labour. The function of the Panel, as defined in Section 86p of the Workers' Compensation Act of Ontario, is as follows:

(a) to investigate possible industrial diseases;

(b) to make findings as to whether a probable connection exists between a disease and an industrial process, trade or occupation in Ontario;

(c) to create, develop and revise criteria for the evaluation of claims respecting industrial diseases; and

(d) to advise on eligibility rules regarding compensation for claims respecting industrial diseases.

The Panel is required by statute to report its findings to the Workers' Compensation Board of Ontario.

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ON

THE HEALTHY WORKER EFFECT

Industrial Disease Standards Panel

IDSP Report No. 3

Toronto, Ontario

June, 1988

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Ontario Ministry of Labour
Ministère du Travail de l'Ontario

Industrial Disease Standards Panel
Comité des normes en matière de maladies professionnelles

10 King Street East
7th Floor
Toronto, Ontario
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June 21, 1988

Dr. R. G. Elgie
Chairman
Workers' Compensation Board
2 Bloor Street East, 20th Floor
Toronto, Ontario
M4W 3C3

Dear Dr. Elgie:

In a letter dated June 12, 1986, the Board requested the Industrial Disease Standards Panel to comprehensively review the issue of the Healthy Worker Effect (HWE) and develop appropriate recommendations for the interpretation of epidemiological studies.

The Panel is pleased to send to the Board its Report of Findings in this matter in accordance with Section 86p(10) of the Workers' Compensation Act. The Panel is in unanimous agreement concerning all of the conclusions contained herein on the consideration to be given to the HWE in the evaluation of epidemiological studies whose results will be used to assist in the adjudication of compensation claims for industrial disease.

The Panel found that the HWE should be taken into account in evaluating such epidemiological studies. Each of these studies should be evaluated on its own merits and, where appropriate, a recommendation and related observations (which the Panel itself will follow) are provided for dealing systematically with the HWE, when it is detected in historical cohort studies, for non-cardiovascular disease causes of mortality (or morbidity).

The Panel will be pleased to respond to questions the Board may have about its findings.

Yours sincerely,

J. Stefan Dupre
Chairman

JSD/dc

Ontario Ministry of Labour

Ministère du Travail de l'Ontario

Industrial Disease Standards Panel

Comité des normes en matière de maladies professionnelles

10 King Street East
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June 21, 1988

MEMORANDUM TO: **WORKERS' COMPENSATION BOARD**

FROM: **INDUSTRIAL DISEASE STANDARDS PANEL**

RE: **REPORT ON THE HEALTHY WORKER EFFECT**

1.0 ISSUES:

1.1 In a letter dated June 12, 1986, the Workers' Compensation Board requested that the Industrial Disease Standards Panel comprehensively review the issue of the Healthy Worker Effect (HWE) and develop appropriate recommendations for the interpretation of epidemiological studies the results for which will, in turn, be employed to develop adjudicative criteria for the compensation of industrial disease. In particular, the Board requested responses to the following questions:

1. Should the WCB take the HWE into account in evaluating the epidemiological data found in mortality and morbidity studies?

2. If the answer to question 1. is yes, then

   a) What type of correction factor should typically be employed to address this potential source of bias?
   b) Are there any sorts of mortality or morbidity outcomes (e.g. cancer) in respect of which this correction factor should not apply?

2.0 PANEL INVESTIGATIONS:

2.1 The significant literature on the HWE has been assembled in the Evidentiary Base (listed in Appendix B), some of which was reviewed in a staff paper (Gallina, 1986) prepared for the Panel. The Panel then decided to obtain advice from a noted epidemiologist, Dr. Geoffrey Howe, Director of the Epidemiology Unit for the National Cancer Institute of Canada at the University of Toronto, in the form of a presentation, discussion and paper (Howe, 1987). A summary of the methodological details in Howe's paper formed the basis for a request for short papers

on the HWE from a number of epidemiologists with international stature. The following material was requested:

a) Examples of the presence of the HWE from the respondent's own occupational epidemiological studies (both mortality and morbidity) and the means employed to deal with it;

b) The knowledge the respondent derived about the HWE therefrom; and

c) The conclusions the respondent now believes to apply about this phenomenon, particularly in the case of cancer.

2.2 As a result, the Panel received ten papers in all from contributors in five countries (four from Canada, three from the United States, and one each from Great Britain, Sweden and Australia). Nine of these papers form Appendix A of this Report. The tenth, by Professor R. S. Roberts of McMaster University, was subsequently withdrawn by the Panel from its Evidentiary Base because the paper's release to Panel had not been fully cleared with its co-authors and sources of information by Professor Roberts. The respondents and their affiliations are listed below:

1. Axelson, O. Dept. of Occupational Medicine, University Hospital, Linkoping, Sweden.

2. Doll, Sir Richard. Imperial Cancer Research Fund Cancer Epidemiology and Clinical Trials Unit, Radcliffe Infirmary, Oxford, United Kingdom.

3. Enterline, P.E. Department of Biostatistics, School of Public Health, University of Pittsburgh.

4. Howe, G.R. Epidemiology Unit, National Cancer Institute of Canada, University of Toronto.

5. McMichael, A.J. Department of Community Medicine, University of Adelaide, Adelaide, South Australia.

6. Miettinen, O.S. Department of Epidemiology and Biostatistics, Faculty of Medicine, McGill University, Quebec.

7. Monson, R.R. Harvard School of Public Health, Boston, Mass.

8. Nicholson, W.J. Division of Environmental and Occupational Medicine, Mount Sinai School of Medicine, New York.

9. Sterling, T.D. School of Computing Science, Simon Fraser University, British Columbia.

2.3 Lastly, the Panel received a compendium of these short papers on the HWE (Heller, 1988).

3.0 PANEL FINDINGS AND RECOMMENDATIONS:

3.1 McMichael defined the HWE as "the consistent tendency for actively employed people to have a more favourable mortality (or morbidity) experience than the population at large". "The HWE is not an intentional measurement of the relative good health of a working population; nor does it quantify the beneficial effects of the occupational environment upon those working within it. Rather, it is an unintended bias, of uncertain magnitude, in an unavoidably imperfect comparative measure of the health status of the working population." (McMichael, 1987)

3.2 The HWE is to be expected in an epidemiological study with a historical cohort design in which the health experience of an employed group is compared with that for the general population. If a comparison with another working group (with similar health status) were possible, then the HWE would not appear. All contributors agreed that the HWE is the result of:

- selection bias (both by employers and by employees at the time of hire and afterward);
- classification bias; and of
- confounding effects (between the observed worker population and the referent population).

A few contributors noted a specific kind of selection bias in the form of a survivor effect which produces a reduced mortality after a longer period of time beyond hire among workers in a known setting of occupational risk.

3.3 Selection bias occurs for various reasons. Employment naturally screens against illnesses which occur at younger ages and which prevent or modify continuing work. However, employment for younger people does not discriminate against diseases of older ages (such as cancer). Nor does it discriminate against diseases for which no clinical manifestations have revealed themselves. Pre-employment medical screening by the employer in favour of robustness (for jobs requiring physical exertion) and against known risk factors among applicants would necessarily lead one to expect deficits in mortality (or morbidity) for some

time following hire in cardiovascular or cerebrovascular disease, and for various other non-malignant diseases (e.g. non-malignant diseases of the respiratory, digestive, endocrine and urinary systems). Unless screening against smoking and dietary fat intake and workers with previous diagnoses of cancer took place, there is no known underlying biological mechanism to explain reduced cancer risks in the years after the first period of employment.

3.4 Selection bias can continue to operate during employment. It is recognized that work confers a number of health-enhancing benefits including income, self-esteem, access to employer-sponsored quality medical care or occupationally conferred health benefits.

3.5 Less well known perhaps is the selection bias caused by the survivor effect in some industries with known occupational risks. In such industries, a lesser mortality for occupationally-related causes of death can occur with prolonged follow up. This appears to occur for two reasons. There is a decline in the number (and proportion) of workers with associated risk factors (e.g. smoking among asbestos workers) in the course of longer employment. As a result, the remaining workers show a less severe occupational risk estimate when compared to a standard population. Another reason for a continuing selection bias would be individual worker susceptibility where the departure of those susceptible would lead to a reduced worker population with a less unfavourable health experience.

3.6 Classification bias can occur when differences arise between the methods used to establish the data for both the worker and reference populations. These include differences in diagnostic criteria, in the quality of death ascertainment and in the quality of data recording. Poor industrial hygiene data can lead to the assignment of workers into incorrect exposure categories.

3.7 Confounding is the result of external factors whose effect can, perhaps, be controlled for during the data analysis. The use of inappropriate comparison rates can lead to confounding. Geographically corresponding rates are more appropriate for use in comparisons with the worker population and usually result in a lessening of the apparent HWE. However, local rates can be inadequate because the small numbers contribute an inherent lack of stability. The date of hire can be used to control for an apparent HWE. Thus, workers hired during World War II or during labour shortages tend to be less fit and less healthy than would otherwise be the case. Other potentially confounding factors include: age at hire, sex, specific cause of death, specific occupation, socioeconomic or social class.

3.8 One respondent suggested using a single parameter to adjust for the presence of the HWE. He based his contention principally on his reanalysis of the Dorn study data (Kahn, 1966) which traced the mortality experience of a cohort of U.S. veterans (principally, World War I veterans) who held active government life insurance policies in December, 1953. It was conducted to determine the relationship between tobacco use and mortality experience. The policyholders were white males drawn from the middle and upper socioeconomic classes. Using the U.S. national population as a basis for comparison, the respondent found that the relative risk of mortality from all causes and from all cancers was reduced. His conclusions concerning the use of a single parameter to adjust for the HWE arose principally for two reasons: the Dorn study group was incorrectly regarded as a typical occupational cohort; there was no control for the confounding factors of socioeconomic class and race.

3.9 Ideally, the reference population used to generate risk estimates should be as closely matched as possible to the worker population. This can be achieved externally using another employed population, or internally using comparisons between high and low exposure groups within the same cohort. Although randomized clinical trials (RCTs) have been singled out as the paradigm for epidemiologists, when considering questions of causation, indirect means of duplicating RCT study designs must be used in occupational epidemiological studies since they are observational by definition.

3.10 Most contributors suggested incorporating a latency period (of from two or three years to twenty years) into the determination of estimates for all cancer standardized mortality ratios (SMRs) or site-specific cancer SMRs.

3.11 With these observations in mind, the Panel makes the following recommendations:

RECOMMENDATION 1: **THE WORKERS' COMPENSATION BOARD SHOULD TAKE THE HEALTHY WORKER EFFECT (HWE) INTO ACCOUNT IN EVALUATING THE EPIDEMIOLOGICAL DATA FOUND IN MORTALITY AND MORBIDITY STUDIES.**

RECOMMENDATION 2: **EACH EPIDEMIOLOGICAL STUDY, ESPECIALLY OF THE HISTORICAL COHORT TYPE, SHOULD BE ASSESSED TO DETERMINE IF THERE IS ANY EVIDENCE OF THE HWE IN THE FORM OF A REDUCED (I.E. < 100%) STANDARDIZED MORTALITY RATIO (SMR) FOR ALL CAUSES MORTALITY OR FOR ALL CARDIOVASCULAR DISEASES MORTALITY; OR CORRESPONDINGLY REDUCED STANDARDIZED MORBIDITY RATIOS (SMbR).**

RECOMMENDATION 3: **A CORRECTION FACTOR SHOULD NOT BE EMPLOYED TO ADDRESS THIS POTENTIAL SOURCE OF BIAS SINCE EACH STUDY REQUIRES INDIVIDUAL INTERPRETATION CONCERNING THE EXTENT TO WHICH THE HWE MAY HAVE BIASED THE POINT ESTIMATE OF THE STANDARDIZED MORTALITY OR MORBIDITY RATIOS FOR EACH CONDITION OF INTEREST.**

RECOMMENDATION 4: **WHERE THERE IS EVIDENCE OF THE PRESENCE OF THE HWE, AND THERE IS THE POSSIBILITY OF EXCESS MORTALITY (OR MORBIDITY) FROM NON-CARDIOVASCULAR DISEASE CAUSES, THE EPIDEMIOLOGICAL ESTIMATES OF MORTALITY OR MORBIDITY SHOULD IN GENERAL BE DERIVED AFTER REMOVING FROM THE ANALYSIS THE INITIAL GROUP OF YEARS FROM THE TIME OF FIRST EMPLOYMENT. THE NUMBER OF YEARS OF FOLLOW UP TO BE SO REMOVED SHOULD BE APPROXIMATELY EQUAL TO THE AVERAGE ESTIMATED DURATION IN TIME FROM THE EARLIEST CLINICAL MANIFESTATIONS OF THE DISEASE TO FINAL OUTCOME (BASED, FOR EXAMPLE, ON THE USE OF SURVIVAL CURVES). FOR LUNG CANCER, FOR EXAMPLE, IT IS SUGGESTED THAT THE INITIAL 5 YEARS FOLLOWING FIRST EMPLOYMENT SHOULD BE REMOVED FROM THE ANALYSIS.**

3.12 Panel considers that all of the above recommendations concerning the manner in which the Workers' Compensation Board should take the Healthy Worker Effect into account in evaluating epidemiological data should apply to Panel in its own work.

APPENDIX A

CONTRIBUTED PAPERS

ON

THE HEALTHY WORKER EFFECT

APPENDIX A

CONTRIBUTED PAPERS ON THE HEALTHY WORKER EFFECT

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OBSERVATIONS ON POSSIBLE SOURCES, EXTENT, PERSISTENCE, CONSTANCY, AND CORRECTIONS FOR THE HEALTHY WORKER EFFECT

VIEWS ON THE HEALTHY WORKER EFFECT AND RELATED PHENOMENA

by

Olav Axelson, Department of Occupational Medicine,
University Hospital, Sweden

The mortality or morbidity experience of a working population is often found to be less than that of a general population, a phenomenon usually referred to as the healthy worker effect. This concept was earlier discussed by McMichael (1976) and has become a popular and loosely used term in epidemiology without much distinction as to the underlying mechanisms. There are several different explanations to consider in this respect, however, some of which occur in some situations but not in other contexts.

SOME THEORETICAL REMARKS

Most important for the appearance of a healthy worker effect is probably the selection of healthy individuals for employment, either actively by the employer or through self-selection. It is likely also that the more qualified the job, the more probable is the occurrence of a strong healthy worker effect through selection. This viewpoint also implies that the healthy worker effect could be low or nonexistent in some unqualified jobs. Furthermore, good health is also promoting an employment to continue, and the complimentary aspect may be true as well.

There might also be various external causes or study-related reasons for the phenomenon to appear in a particular study. For example, regional differences in the occurrence of certain disorders may contribute in this respect, e.g. if the worker population belongs to a region with better health than the country at large. Also the reversed situation may be at hand but would not attract much attention as the healthy worker effect would then be decreased and obscured. There might be even more spurious reasons behind the appearance of a healthy worker effect, however. For example, the regional differences in the occurrence of a particular disease may be perhaps influenced by the quality of the health care as well as of local peculiarities in diagnostic criteria or terminology. This might contribute to the overall healthy worker effect seen in a study, i.e. there is rather a "pseudo-healthy" worker effect as having nothing to do with good health of workers but rather with bias.

Selectional errors may occur and distort what is known as the study base, i.e. the specific population-time segment that is involved in any particular study, and from which the information is harvested (Miettinen 1982). Such selection phenomena may take place through various mechanisms, also long before any investigation is even planned, but may

also be the direct result of inadequate design or study procedures. For example, the material of subjects for a study would be inadequate if dead individuals were sorted out from company records or from trade union registers, which might be used for the study. Then the result would be a rather strong undermortality without any clear effect from the exposure even if existent. Such a selection error could be the result of a reconstruction of a company, i.e. the active work-force of a department or some other sector of a factory could have entered a new registry at a particular time, whereas deceased or sick individuals may not have been transferred to the new register in the same manner. Afterwards such circumstances may be difficult to reveal and the subsequent bias in the study might go undetected and be mistaken for a healthy worker effect.

There is also another issue of validity, which deserves attention and which has to do with the character of the reference population, i.e. when there is a specific such population for comparison (rather than numbers of expected cases as derived from national rates). Hence, also another industrial population, than that under study, i.e. a tentative reference population, could have some totally different exposure, that might cause the same disorder(s) as the exposure under study. For example, the choice of a group of copper smelter workers (even matched on smoking, etc.) as a reference population for miners would fail to reveal any actual excess risk of lung cancer, since radon daughter exposure in the mines, and arsenic exposure in the copper smelter would both cause lung cancer in excess (cf. Pershagen 1985). Again, a comparison in this respect would result in some degree of a pseudo-healthy worker effect, which may or may not be seen in the data of the study.

It is also quite obvious that the reference population should not come from an urbanized area if the index population is rural, or the reverse, especially if lung cancer or some other type of tumour or disease, as more frequently occurring in urban areas, is under study. Similar considerations are always necessary, but the circumstances may be less obvious than in these examples, especially when it comes to studies of moderate increases in disease rates or mortality with regard to widespread but rather diffuse exposures. The full effect of an agent causing cancer may therefore not be revealed in rural populations because any (broader) comparison group tend to involve sectors of an urbanized population as often having an increased risk of various cancer forms.

The principles for good comparability of populations are well appreciated for cohorts, and the healthy worker effect is usually thought of as reflecting a deficiency in this respect, but similar aspects should also apply to case-referent studies. Hence, it is questionable to just consider one particular exposure in case-referent studies, disregarding the fact that other, more or less ill-defined determinants of the disorder may operate in the unexposed sector of the study base (i.e. a situation that may also be seen as one of negative confounding). Instead it is important to try and identify an unexposed

sector of the base, which is believed to be at least free from a priori known determinants of the disease and to use this subpopulation as the reference. For example, should miners and copper smelter workers live in the same area, it is necessary to identify and separate these categories and to use the remaining population sector as the reference category for estimating risk in any of these occupations (cf. Pershagen 1985 for an example).

EXAMPLES AND EXPERIENCES

By allowing for some latency time from first exposure to start of observing deaths or cancer cases, the healthy worker effect is usually decreased, since the good health at first employment gets lesser and lesser influence with time. For example, in a cohort of workers exposed to trichloroethylene, a requirement of 10 years of latency changed the observed to expected numbers from 49/62.0 to 37/39.8 for total mortality and from 11/14.5 to 9/9.5 for all tumors (Axelson et al 1976). This experience may be a simple illustration of what usually happens when allowing for latency time. This may even be done indirectly by considering the observed to expected number of deaths or cancers in various time periods after first exposure.

A further illustration of the healthy worker effect phenomenon can be obtained from a study by Ott et al (1983), who studied the workers of two factories with the same type of production but one of them not using the agent of interest, namely methylene chloride. Both populations showed nothing but strong healthy worker effects in comparisons to expected numbers based on the national cause-specific mortality, but interestingly, the workers with the exposure had a higher cardiovascular mortality compared to the others. Although the numbers were small and the two factories located in different states in the U.S., this comparison of two seemingly well comparable populations indicated the possibility that methylene chloride could be a risk factor for cardiovascular disease (say, by its metabolism through carbon monoxide).

A further illustration of the healthy worker effect might be obtained from two cohort studies on herbicide exposure (Axelson et al 1980; Riihimaki et al 1982). One of them had some excess of cancer and a slight healthy worker effect for other causes of death, the other showed a very strong healthy worker effect as even increasing for cancer with a strengthening of the latency time requirement (one observed versus 5.7 expected with 15 years of latency; $P < 0.05$ for prevention). The interpretation would have to be that there is either a real prevention or, perhaps more likely, a selection bias explaining the figures obtained (an overall interpretation of these and other studies on herbicides is another matter as not attempted here at all).

In case-referent studies, a healthy worker effect may also be seen, for example in the younger age strata in a study of exposure to nitroglycerine and nitroglycol exposure in the explosives industry (Hogstedt and Axelson 1977), in this case presumably an effect of rather rigorous pre-employment health check-ups. No particular efforts seemed

possible to specifically deal with this phenomenon, since no other design involving a comparison with similarly selected group was possible. On the other hand, in older ages there was a clear increase in cardio-cerebrovascular deaths.

Sometimes a restriction of the study base underlying the cases of a case-control study may be helpful. A study design illustrating this point may be seen in a study of neuropsychiatric disorders and solvent exposure, where a restriction of the study base was done so as to involve only individuals with employment in construction activities, e.g. excluding white-collar workers as well as farmers, forestry workers and other groups where the frequency of especially mental disorders as a reason for pre-time pensioning was likely to be different for one reason or another (Axelson et al 1976).

SOME CONCLUDING REMARKS

With regard to positive studies, the healthy worker effect is less problematic to deal with although resulting in a lowered risk. The problem comes instead in the non-positive or negative studies, where the question arises whether there is no effect of the exposure or if a moderate effect has been obscured through the operation of a healthy worker effect or some other more or less related phenomenon. The application of some adjustment factor to the expected numbers could be thought of, but any suggested magnitude of a correction would hardly be generally accepted. The application of an adequately long latency period, or an analysis comparing observed and expected cases in various periods of time since first exposure, may be helpful in decreasing the influence of the healthy worker effect, at least in cancer studies, where the early exposure may play the greater role. Usually, however, the healthy worker effect has to be dealt with on a judgmental basis and to the extent that there is no clear excess of disease, that is strong enough to break through this effect, no positive conclusions can be drawn (but obviously no conclusions about a lack of effect either).

The radical solution of the problem of the healthy worker effect would in principle be to use a proper comparison group whenever possible. Still, it will probably be unavoidable also in the future, for economic and other reasons, to calculate expected numbers from national or regional rates for comparison with the observed number of cases, even if such a study design is known to be less adequate, not to say inadequate from a scientific standpoint (cf. Wang & Miettinen 1982).

However, even an opposite view may be taken because of the difficult problem to know what reference group that would be proper, and therefore there is perhaps some justification for using national rates in the context of cohort studies in spite of the problems caused by the healthy worker effect. This might be especially true for cancer studies since the healthy worker effect is usually moderate for cancer. For case-referent studies, the corresponding justification would be to have just all nonexposed as the reference rather than a particular sector of these. The comparison population might therefore in both instances be

thought of as a reasonable average for comparison and evaluation of overmortality or overmorbidity in general, more or less leading to a sort of ethical point of view regarding the risk taken by a particular worker population. This could be relatively adequate from the point of view of the society, but not necessarily so for the exposed individual or a worker group. This view is not in agreement with the principles argued above, however, and does not lead to a clear scientific evaluation of agent-specific effects. A reasonable and practical compromise could be therefore, to apply at least some refinement as discussed, e.g. to exclude white collar professions as easily done in a case-referent design regarding some exposure in blue-collar work. This is in contrast to the possibilities in cohort studies, since national rates inevitably include all kinds of professions as well as unemployed with their high mortality, and the resulting problems of comparability. Rates for social subgroups of a population could therefore be desirable but are rarely available.

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HEALTHY WORKER EFFECT

by

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INTRODUCTION

I first became aware of the complication that the so-called "healthy worker effect" introduces into studies of occupational mortality in 1965, when I analyzed data that had been collected in a study of coal gasworkers employed by four of the British Area Gas Boards (Doll et al., 1965). All men were included in the study who, on 1 September, 1953 were aged between 40 and 65 years of age, had selected occupations, had been employed by the industry for more than five years, and were currently in employment or in receipt of a company pension. The last, rather unusual, criterion (being in receipt of a company pension) was included to ensure that the results were not biased by the exclusion of men who had retired early on grounds of ill-health. Altogether 11,499 men were included and all but 50 (0.4%) were followed successfully for 8 years or until death, whichever was the earlier. The 50 untraced men were assumed to have been alive so that the recorded mortality rates may have been (and in fact were) slightly underestimated. The men were divided into three broad occupational categories according to whether they had heavy, intermittent, or no exposure to the products of coal carbonization and their mortality from all causes and ten specific causes or groups of causes was compared with that expected if the men had the same mortality rates as all men in England and Wales of the same ages over the same period. The results are shown in Table 1. They showed the anticipated occupational hazards (of cancers of the lung, bladder, and scrotum for the heavily exposed workers) and suggested hazards of bronchitis for the heavily exposed men and of pneumoconiosis for the maintenance men. They also showed, however, a reduced mortality from arteriosclerotic and degenerative heart disease and from a residual group of other causes in all three occupational groups (Standardized Mortality Ratios* of 75, 79, and 82 and of 83, 86, 73) and a substantially reduced mortality from all causes for the men with intermittent or no exposure (SMRs of 90 and 84).

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* Abbreviated subsequently to SMRs.

The first explanation for the reduced mortality rates that we considered was that the comparison with national rates was inappropriate and we, therefore, re-examined the results, comparing the observed mortality in each Area Board with that observed in the corresponding regional conurbations, choosing the regional conurbation for comparison rather than the region as a whole on the grounds that the great majority of the gasworkers lived in the large conurbations. The results showed that the low mortality rates in the men with intermittent and no exposure could not be wholly attributed to the choice of national rather than local rates for comparison; but they did show that the low mortality from occupational causes of death was limited to two of the four geographical groups (Table 2).

Our discussion of the reasons for these low mortality rates is perhaps of some interest, as it was one of the first to have been published: that is, apart from the many previous discussions of the low mortality commonly observed in the first year or two after recruitment of an active population that was known to occur as a result of selective factors that excluded some of the seriously ill. I have, therefore, quoted it in full:

> "The reason for the low mortality from all other 'non-occupational' diseases is also unexplained. It is not due to a beneficial effect of heavy physical work in retort houses, since it is observed among all types of employee...; nor is it an attribute of the industry as a whole, since it is observed among the employees of only two of the four Boards.... One explanation might be that the mortality in two of the Boards was underestimated as a result of recording some men as alive who were in fact dead. A check on a randomly selected 10% sample at Board III failed, however, to indicate that any substantial number of deaths could have been missed. The status of all but one of the men was confirmed; this man was said to have been still employed by the Board, whereas he had actually left though he was still alive. If the explanation is that some deaths have been missed, the mortality from occupational diseases is presumably also underestimated.
>
> An alternative explanation is that some selective bias resulted in the inclusion of a relatively healthy group of employees in two of the Boards. Work in horizontal retort houses is heavy, and it would be understandable if chronic invalids failed to qualify for inclusion in the study by continuing to work for five years. It is, however, difficult to see why such a bias should affect men employed as meter collectors, meter readers or gas fitters (class C).* The high rate of employment in the south east may perhaps have resulted in a more rapid labour turnover among

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* The group described here as having "no exposure"

unhealthy men, but if this were the explanation we should have anticipated that the bias would have worn off after the first few years of follow-up. In fact the mortality from non-occupational causes was practically the same in the first three and in the last five years of the study (Board III, 9.6 and 9.4 per 1,000; Board IV, 8.2 and 9.1 per 1,000 respectively).

Whatever the explanation, it is difficult to see how the deficiency could have produced a spuriously high mortality from occupational diseases, which, it may be noted, was raised in all four Boards. It is not, we think, reasonable to suggest that the deficiency of deaths from non-occupational causes is due to bias in favour of diagnosing cancer of the lung or bronchitis. First, the deficiency is apparent in all three occupational classes, whereas the excess mortality from lung cancer and from bronchitis is present only among class A workers. Secondly, the causes of death have been classified according to the information given on death certificates; these were completed by many different doctors who were unaware of the existence of the present study and not likely to be biased by knowledge of the subjects' occupation."

PERSONAL EXPERIENCE

Since reporting this work my colleagues and I have obtained mortality data for many other groups of workers, some of which are the results of continued observations on workers whose mortality we had reported previously. I have preferred, however, to cite the latest data, even if they are still unpublished, as the larger numbers reduce the element of random variation. To these I have added data on two very large groups of workers that I have analyzed recently at the request of the European Office of the World Health Organization and of the Chemical Manufacturers Association (on, respectively, men and women manufacturing man-made mineral fibers and men exposed to vinyl chloride). These two sets of data were not collected by me or my colleagues, but many of the data are still only in press, the reviews are original, and I thought that the results would be of interest as they relate to so many workers followed for long periods.

Table 3 lists the studies and the types of disease that were found to be (or suspected of being) specifically associated with the occupations under investigation. Deaths attributed to the diseases listed are excluded from the data presented in Tables 4 and 5. A very brief account of each study is given in an Appendix.

Table 4 shows, for each study, the SMRs for all cancers combined, other than those listed in Table 3, derived from the numbers of deaths that would have been expected had the workers experienced the same mortality

rates as all men and women of the same ages in the country as a whole over the corresponding periods. In some instances it has also been possible to include SMRs corrected for locality, by the use of regional or county rates or by the use of correcting factors derived from knowledge of the difference between national and local rates for the group of diseases concerned. Inspection of Table 4 shows that the SMRs for cancers not known to be related to the various specific occupations, are nearly all close to 100. Eight are greater than 100 and five are less than 100. Only one difference is statistically significant (the deficiency of cancers other than cancers of the lung and mesothelioma in male textile asbestos workers) and that is only marginally so (P=.02 when compared with national rates and .04 when compared with local rates).

Table 5 shows SMRs for all non-occupationally induced diseases other than cancer in the same 10 occupational groups plus radiologists, whose experience could not be included in Table 4 because all types of cancer (except possibly chronic lymphatic leukaemia) are believed to be induced by exposure to ionizing radiations. The data are limited to deaths from non-malignant diseases, excluding, whenever possible, deaths due to injury and poisoning, as this latter group will inevitably include an unknown proportion attributable to industrial accidents. Diseases due to non-malignant diseases certainly or possibly due to hazards associated with the specific occupations are also excluded (see Table 3). The results are substantially different from those in Table 4. Six SMRs are greater than 100, one equals 100, and 14 are less. In many instances moreover, the differences are statistically significant. Four excesses are significant (the excess of deaths due to diseases of the circulatory system in nickel salt manufacturers, of respiratory disease (other than asbestosis) and of circulatory disease in asbestos textile manufacturers, and of diseases other than circulatory disease in mustard gas workers). In three instances, however, the excess disappears or becomes statistically non-significant when a correction is made for the locality of the factory. Whether it would disappear in the fourth (non-malignant diseases other than circulatory disease in mustard gas workers) depends on whether it is more appropriate to compare the workers with the population of Cheshire Urban Districts (in one of which the factory was situated) or with the population of neighboring Merseyside, whence many of the workers are likely to have been drawn. Of the 14 SMRs less than 100, eight are significantly low. Unfortunately, correction for locality or, in the case of radiologists for social class, could be made for only three. In one instance the deficiency ceased to be statistically significant (circulatory disease in nickel foundry workers) in one it became marginally significant (all non-malignant diseases in radiologists) and in one it remained highly significant (diseases other than circulatory disease in nickel foundry workers).

DISCUSSION

In interpreting these and other similar results, we need to take the following into account:

1. The low mortality rates reported in many occupational cohort studies are partly an artifact due to incomplete follow-up, inaccurate information, and the failure to obtain information about the cause of death for all workers known to have died. This is not a major factor, but it is certainly one of the reasons why low SMRs are often reported. In our own study of gasworkers (Doll et al., 1965) we initially failed to trace 50 out of 11,499 men (0.4%) as noted above. A continued follow-up (Doll et al., 1972) found that 5 of the untraced men were dead, 7 others who had been reported as alive and in receipt of a company pension had also actually died before the end of the stated period, and 3 others had died who had been reported as alive (although not in receipt of a pension). In total the mortality rate should have been increased by 1.2%. Failure to obtain information about the cause of death is uncommon in British studies, but it is common in US studies, which require searching for death certificates in up to 50 States. When all three types of error are allowed for (incomplete tracing, erroneous reports, and failure to trace death certificates) it would not be surprising if many studies (with follow-up rates of the order of 95% or less) underestimated SMRs by 5 or occasionally even 10%.

2. Low SMRs derived by comparing the experience of a cohort with that of the whole country may be misleading, because the national standard may have been inappropriate. When a factory is in a highly industrialized zone the SMRs may be overestimated (particularly in the case of lung cancer) but low SMRs for respiratory and circulatory disease may well be due to the location of the factory in a relatively low risk area, as was the case with our nickel foundry workers.

3. After these factors are allowed for, it still remains true that SMRs for non-malignant disease are commonly found to be well below 100 in occupational studies, a deficiency that has been attributed to the "healthy worker effect". At least four factors contribute to it:

   (i) selection by the employer to exclude those obviously at high risk, e.g. individuals suffering from chronic bronchitis and emphysema, congenital heart disease, gross obesity, alcoholism, and psychosis, or convalescent from the treatment of a potentially fatal disease, etc. Some of this selection wears off within a couple of years, but much of it persists for decades.

(ii) selection to exclude those whose ill health makes the work unsatisfactory or uncongenial. In so far as this leads to people giving up work within a few months it will affect all studies which include only people who have worked for a minimum specified period. The longer the qualifying period for entry to the cohort, the more likely it is for workers with poor health to be excluded. This is particularly important if the great majority of workers included in a cohort are already in employment at the start of the study and becomes progressively less important as the proportion of the cohort recruited after the start of the study increases.

(iii) self selection by workers who, by virtue of their personal characteristics (for example, a tendency to alcoholism) change jobs frequently. Nearly all occupational studies exclude very short term workers; most exclude individuals who have worked for less than 6 months, many exclude those who have worked for less than a year, and a few concentrate on individuals who have worked for 5 years or more, with the intention of ensuring that those studied have had prolonged exposure to the suspect hazard. Evidence that short-term workers tend to have high mortality rates from many non-malignant diseases is accumulating and the exclusion of such workers inevitably results in some low SMRs.

(iv) a beneficial effect of work. This includes not only the benefit of employment as compared to unemployment (which, there is increasing evidence to suggest, is in itself harmful to health) but also such effects as still occur in some industries, like the beneficial effect of physical exertion in reducing blood pressure and the risk of myocardial infarction.

It is not, of course, to be expected that these factors will always have the same effect even after artifacts have been excluded. Their effects may vary to some extent depending on (a) the length of time individuals

are followed (the longer the time, the smaller the effect); (b) the criteria for inclusion in the study (the longer the period of employment required, the greater the effect) and (c) the social conditions at the time of employment (for example, cohorts that include a substantial proportion of men recruited during periods of high employment and, particularly during the second world war, are less likely to have excluded individuals at high risk of sickness). Whether the factors referred to in paragraph 3 have much effect on the SMR for cancer is another matter. A few certainly will, such as the exclusion of alcoholics. This effect, however, is likely to be small and in general it is doubtful whether the selective factors that reduce the SMR for non-malignant diseases will have any corresponding effect on the SMR for cancer. A recent history of (say) gastric or lung cancer will certainly reduce the opportunities for starting a new appointment, but the effect of this sort of selection will mostly wear off within two years. It is extremely difficult to predict who will get cancer (apart from knowledge of the individual's smoking habits) and, unless there is selection against smokers, it is not evident that any of the factors referred to in paragraph 3 will have any material effect on the risk of cancer after (at the most) 5 years.

Experience of industrial cohorts shows that the SMR from cancers other than those known to be due to occupational hazards are most commonly close to 100 and that this also pertains when no specific occupational cancer hazard exists. In some cohorts, of course, a relatively high SMR for cancers not known to be due to occupational hazards compared to the SMRs for non-malignant diseases can be due partly to the misdiagnosis of cancers of other types that are known to be occupationally induced (as certainly used to happen with mesotheliomas in asbestos workers and probably still also occurs whenever there is a peculiarly high incidence of lung cancer) and partly to a more widespread effect of a carcinogen than has been recognized (as might be the case with vinyl chloride). In these circumstances, however, the SMR for other cancers is likely to be over 100.

CONCLUSION

I conclude that the healthy worker effect is a real phenomenon, but that it is irrelevant to the interpretation of SMRs for cancer in occupational studies, so long as the first five years' observations after recruitment to the study are excluded.

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Table 1

MORTALITY OF GASWORKERS COMPARED WITH NATIONAL EXPERIENCE

(Doll et al, 1965)

Cause of death	SMR for men with		
	heavy exposure	intermittent exposure	no exposure
Occupational causes			
Cancer of lung	169	113	100
" " bladder	221	143	57
" " skin and scrotum	350	0	0
Possible occupational causes			
Bronchitis	213	99	94
Pneumoconiosis	71	186	0
Other causes			
Other respiratory disease	104	77	92
Arteriosclerotic and degenerative heart disease	75	79	82
Other disease	83	86	73
Injury and poisoning	106	88	79
All causes	105	90	84

Table 2

MORTALITY OF GASWORKERS COMPARED WITH REGIONAL EXPERIENCE

(Doll et al., 1965)

Gas Board		SMR for men with		
		heavy exposure	intermittent exposure	no exposure
1	Occupational*	179	62	65
	Non-occupational**	97	97	91
2	Occupational	136	103	68
	Non-occupational	107	110	90
3	Occupational	145	113	77
	Non-occupational	76	77	79
4	Occupational	162	79	91
	Non-occupational	58	70	78

* Including possible occupational causes, see Table 1.
**Including injury and poisoning, see Table 1.

Table 3

STUDIES REVIEWED

Authors	Occupational groups studied	Occupational hazards
Doll et al., 1965 " " 1972	Gasworkers exposed to combustion products of coal	Cancers of lung, bladder, skin and scrotum. Bronchitis (?)* Pneumoconiosis (?
Doll et al., 1977	Nickel refiners	Cancers of nasal sinuses & lung
Easton et al., 1988a	Nickel salt manufacturers	Cancer of lung (?)
Easton et al., 1988b	Nickel foundry workers	Cancer of lung (?)
Wald et al., 1984	Hydrazine manufacturers	Cancer of lung (?)
Peto & Doll, 1985	Asbestos textile workers	Cancer of lung & mesothelioma. Asbestosis
Al-Dabbagh et al., 1986	Nitrate fertiliser manufacturers	Cancer of stomach (?)
Easton et al., 1988c	Mustard gas workers	Cancers of buccal cavity, pharynx, nose, larynx & lung.
Smith & Doll, 1981	Radiologists	Cancers of all sites
Doll, 1987a	Man-made mineral fibre workers	Cancer of lung
Doll, 1987b	Vinyl chloride workers	Cancer of liver (angiosarcoma)

*Hazards marked with a query (?) were suspected but unproven.

+In maintenance men with intermittent exposure.

Table 4

MORTALITY FROM CANCERS OTHER THAN THOSE SUSPECTED OF ASSOCIATION WITH THE OCCUPATION UNDER INVESTIGATION

(numbers of deaths in parentheses)

Occupational group	SMR derived from comparison with:	
	National Mortality	Regional or Local Mortality
(a) Gasworkers - heavy exposure	111 (94)	
intermittent exposure	101 (94)	
no exposure	88 (111)	
Nickel refiners	102 (75)	
Nickel salt manufacturers	96 (16)	
Nickel foundry workers	90 (45)	98
Hydrazine manufacturers	76 (7)	
Asbestos textile workers - men	81 (117)	83
women	105 (15)	
Nitrate fertiliser manufacturers		106 (79)
		(b) 103
Mustard gas workers	106 (284)	(b) 99, (c) 89
Man-made mineral fibre workers	103 (1060)	
Vinyl chloride workers	102 (609)	

(a) Different from the results shown in Table 1 because of the inclusion of additional data from Doll et al., 1972.

(b) Based on local county rates.

(c) Based on neighbouring conurbation rates.

Table 5

MORTALITY FROM ALL CAUSES OTHER THAN CANCER, DISEASES DUE TO THE OCCUPATION UNDER INVESTIGATION, AND INJURY AND POISONING

(numbers of deaths in parentheses)

Occupational group	SMR derived from comparison with: National Rates	Regional or Local Rates
(a) Gasworkers, heavy exposure	95 (345)	
intermittent exposure	86 (340)	
no exposure	79 (414)	
Nickel refiners	(d) 101 (413)	
Nickel salt manufacturers	(e) 144 (75)	116
	(f) 94 (26)	
Nickel foundry workers	(e) 80 (102)	98
	(g) 65 (26)	60
Hydrazine manufacturers	(h) 81 (37)	
Asbestos textile manufacturers, men	(j) 115 (536)	97
"	(e) 130 (169)	93
"	(g) 95 (85)	
women	87 (27)	
Nitrate fertiliser manufacturers		(e) 80 (145)
		(g) 67 (56)
Mustard gas workers	(e) 108 (877)	(b) 103, (c) 91
	(g) 132 (525)	(b) 143, (c) 100
Radiologists registered before 1921	95 (257)	(k) 104, (l) 97
" " after 1920	76 (339)	(k) 89, (l) 87
Man-made mineral fibres	100 (4703)	
Vinyl chloride workers	(d) 84 (1547)	

(a), (b), (c) See corresponding footnotes to Table 4.

(d) Including injury and poisoning. (e) Circulatory disease.

(f) Other diseases and injury and poisoning. (g) Other diseases.

(h) All other diseases and injury and poisoning. (j) Respiratory disease

(k) Compared with men in social class I.

(l) Compared with all medical practitioners.

APPENDIX

1. Coalgas workers (Doll et al., 1965 and 1972)

11,499 men employed by one or other of four area Gas Boards for at least 5 years were followed for 8 years from 1.9.53. All but 50 (0.4%) were traced. The men were all those employed in carbonizing plants (regarded as having heavy exposure to the products of coal combustion), all employed on maintenance work in gas-producing plants and as process men in gas-producing plants other than retort houses (regarded as having intermittent exposure) and all employed as process or maintenance workers in by-products plants, prepayment meter collectors, credit meter readers, and gas fitters (regarded as having no exposure).

A further study included the 2,444 men with heavy exposure and the 579 men who had worked in by products plants (with no exposure) in the first study and an additional 4,687 men, meeting similar criteria to those in the first study, who were employed by four other area Gas Boards. These consisted of 1,176 men with heavy exposure, 1,430 men with intermittent exposure, and 2,081 prepayment meter collectors, credit meter readers, and gas fitters with no exposure. All were followed for four years from 1.9.61. All but one of the total of 7,710 (0.01%) were successfully traced.

In both studies, the observed mortality was compared with that expected from national mortality rates for England and Wales in men of the same ages over the same period and separately, for four groups of diseases, from the mortality rates recorded in the regional constructions which corresponded most closely with the areas covered by the individual area Gas Boards.

2. Nickel refiners (Doll et al., 1977)

967 men who had been employed for at least 5 years in a nickel refinery using the nickel carbonyl process in S. Wales and whose first employment was in or before April 1944 were followed from April 1934 or such other later date as qualified them for 5 years employment to 1 January 1972. All but 37 (3.8%) were traced. The observed mortality was compared with that expected from national mortality rates for England and Wales in men of the same ages over the same period. Earlier reports on subgroups of these men had been published by Doll (1958) and Doll et al. (1970).

3. Nickel salt manufacturers (Easton et al., 1988a)

289 men employed for at least one year in either the wet treatment or chemical products plant at a nickel refinery in S. Wales who had not been employed at the refinery before 1933

(when the hazard associated with the refining process was considered to have been almost or completely eliminated) were followed from the time they qualified for inclusion (some time after 1937 when the plants first opened) to 31.12.85. The observed mortality was compared with that expected from national mortality rates for England and Wales in men of the same ages over the same period. Expected mortality rates from lung cancer and from circulatory disease were also obtained by the use of rates for rural Glamorganshire, where the refinery was located.

An earlier report on these men was published by Cuckle, Doll, and Morgan (1980).

4. Nickel foundry workers (Easton et al., 1988b)

1,907 men employed for at least 5 years in a nickel foundry in Hereford, between its opening in 1953 to April 1978 were followed to 1.4.85. All but 21 (1.1%) were traced. The men were divided into five categories according to the extent to which they were likely to have been exposed to nickel dust and their mortality compared with that expected from the national mortality rates for England and Wales in men of the same ages over the same period. Expected numbers of deaths were also obtained by the use of rates appropriate for the urban areas of Herefordshire, in one of which the foundry was located.

An earlier report on these men was published by Cox et al. (1981).

5. Hydrazine manufacturers (Wald et al., 1984)

427 men employed for at least 6 months in a factory in which hydrazine was produced between 1945 and 1971 were followed from the time they qualified for inclusion to 31.7.82; 21 (5.2%) were untraced. The men were divided into three groups according to the amount of exposure they were likely to have had and their mortality was compared with that expected from the national mortality rates for England and Wales in men of the same ages over the same period.

6. Asbestos textile workers (Peto et al., 1985)

Three groups of men and women employed at a Rochdale asbestos textile factory were followed to 30.6.83, i.e. 145 men first employed before 1933 who had served 20 years or more in scheduled areas, 238 women first employed between 1.1.33 and 31.12.62 who had served 10 years or more in scheduled areas, and 3,211 men first employed between 1933 and 1974, including all who had been employed for at least 5 years with some time in scheduled areas or on maintenance and a 10% sample of all other employees. Men with Asian surnames and men with previous

occupational exposure to asbestos were excluded from this third group. Each group was followed to 30.6.83. 135 (4.2%) of the men in the third group were untraced; none was untraced in either of the other groups. Mortality was compared with that expected from the national mortality rates for England and Wales for men and women of the same ages over the same periods and corrected for the mortality from broad groups of diseases by use of the SMR for Rochdale (the town in which the factory was situated) for 1969-73.

Data for the first group of men employed before 1933 are not shown in this report because exposure to asbestos was so gross that it had a major but unassessable effect on the mortality from respiratory and circulatory diseases other than that recorded as due to asbestosis.

Previous reports on some of these workers have been published by Doll (1955), Knox et al. (1968), and Peto et al. (1977).

7. Nitrate fertiliser workers (Al-Dabbagh et al., 1986)

1,327 men employed for at least one year in the production of nitrate based fertilisers between 1946 and 1981 were categorized as having had high, intermediate, or low exposure to nitrates or nitrogen oxides. All but 2 (0.2%) were followed to 1.3.81. Their mortality was compared with that expected from Northern regional rates for men of the same ages over the same period and the expected deaths were corrected crudely for locality by multiplying by the ratio between the SMRs for the locality and the Northern region in and around 1973.

8. Mustard gas workers (Easton et al., 1988c)

2,498 men employed at a factory in Cheshire in the manufacture of mustard gas at any time between 1.7.38 and 31.12.44 and 1,052 women employed for at least one year at the same factory over the same period were followed from 1.1.45 to 31.12.84: 176 (5.0%) of the total were untraced. Their mortality was compared with that expected from national rates for men and women of the same ages over the same period. The expected deaths were corrected crudely for locality in two ways: by adjusting by the ratio between Cheshire urban and national rates at ages 15-64 years and by adjusting similarly using the neighbouring Merseyside rates instead of the Cheshire urban rates.

A preliminary report about a subcohort of these workers has been published earlier (Manning et al., 1981).

9. **Radiologists** (Smith and Doll, 1981)

All medically or dentally qualified men who joined a British radiological society between 1897 and 1954 have been followed up to 1.1.77, excluding only those who were abroad or in the Colonial or Armed Services at the time of registering with the society. 339 men joined before 1921, when rigorous measures for protection against ionizing radiations were introduced and 999 joined subsequently. All the former group were traced, but 5 of the latter (0.5%) were untraced. The observed deaths were compared with the numbers expected from national mortality rates for (i) all men of the same ages over the same period, (ii) all men in social class I, and (iii) all registered medical practitioners.

An earlier report of the mortality of these same men was published by Court Brown and Doll (1958).

10. Man-made Mineral Fibre workers (Doll, 1987a)

Three cohorts of men and women employed in the production of man-made mineral fibres have been studied in Canada (1 plant), Europe (13 plants) and the USA (17 plants). Altogether information has been obtained about 7,862 deaths in 41,185 workers observed for varying periods between the 1930s and the end of 1982. The results were reviewed by RD at a symposium organized by the European Office of the World Health Organization in October 1986 and the individual papers and the review are in press. Notable difference in mortality were observed between rock and slag wool workers, glass wool workers, and glass filament workers and between the results for lung cancer when mortality was compared with that expected on the basis of national rates and on the basis of local county rates in Europe and the USA. The mortality of Canadian workers was compared only with that expected on the basis of provincial rates.

The full results obtained in the three studies are to be published shortly (Enterline et al., 1987; Shannon et al., 1987; Simonato et al., 1987).

11. Vinyl chloride workers (Doll, 1987b)

The published reports of the mortality of men occupationally exposed to vinyl chloride are reviewed. Material of substantial value has been provided only by four studies: (i) A study of 16,173 men employed in 37 plants in the USA, including all men who had been exposed to vinyl chloride for at least one year between 1942 and 1972 inclusive. Most were followed to 31.12.82, but a few were followed only to 31.12.77: 7.3% were untraced and no cause was identified for 6.3% of the 1,439 who had died. (ii) A study of 5,498 men employed for at

least one year on jobs involving exposure to vinyl chloride between 1940 and 1974 in 9 plants in the UK and followed to 31.12.84: 1.1% were untraced. (iii) A study of 451 men exposed to vinyl chloride by virtue of their employment for at least 5 years in one Canadian plant since 1943 and followed to 31.12.77: all were traced (by initial definition). (iv) A study of 618 men employed for at least 6 months in one or other of two Italian plants between 1953 (when operations began) and 31.12.81 and followed to 31.12.84: 3 (4.9%) were untraced. Certified causes of death were obtained for all the 905 men in the UK, Canadian, and Italian cohorts who had died. In each study the numbers of deaths were compared with the numbers expected if the man's mortality had been the same as that recorded in men of the same ages over the same periods in the whole country or the corresponding province.

The results of the Canadian and Italian studies have been published (Theriault and Allard, 1981; Belli et al., 1986). The results of the US and UK studies are to be published (Environmental Health Associates, 1986; Jones, 1986).

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COMMENTS ON THE "HEALTHY WORKER EFFECT" IN OCCUPATIONAL EPIDEMIOLOGY

by

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In every worker study I have conducted where there has not been a probable occupational hazard all cause death rates have been less than rates expected based on the mortality of populations of the entire United States, of the state in which the worker lived or of the local area where the worker's place of employment was located. Some small part of this deficit could be the failure to track every individual to determine his vital status or due to inaccurate death ascertainment. In general, however, I believe that what is reflected here is simply a selection against ill health for participation in the work force. The extent of selection varies by disease classification with the greatest selection against those diseases that appear early in life, and with little selection against diseases unlikely to be manifest at time of employment. Thus, there is little selection against cancer since for the most part symptoms of this disease appear only a few years before death occurs and deaths from this condition tend to occur late in life. On the other hand there is selection against nonmalignant diseases, particularly cardiovascular disease. This is partly due to the fact that some of these diseases are manifest fairly early in life and prevent labor force participation and partly because these diseases are usually of long duration and interfere with employment during periods of life when individuals are likely to be members of the workforce.

Both the employee and the employer seem to participate in the selection process. Workers who do not have strong motivation to work because of health problems do not present themselves for employment while, historically at least, employers have reserved the right to reject certain persons because of physical disabilities. The extent to which these processes occur varies with time and place. During periods of labor shortages the less fit workers are more likely to be taken into the labor force whereas during periods of labor surpluses employers can be much more selective in deciding who will be employed.

My own studies have been largely confined to manufacturing in what might be considered to be heavy industries. In general I find that workplaces that appear (to me) to be fairly clean and desirable tend to produce workers where the healthy worker effect is greater than workplaces that appear to be undesirable. In a study we recently completed on copper smelter workers we found the standardized mortality ratio for all causes of death to be 86.4 based on 1491 deaths while in a study of workers at a large chemical complex the SMR for all causes of death was 74.7 based on 1180 deaths.

One problem is trying to separate any effects that might have resulted from the employment itself from overall mortality. These effects can be

both negative and positive. While health hazards clearly exist in industry it seems reasonable to suppose work itself brings some satisfaction if only in the form of monetary rewards and the ability to purchase goods, as for example medical care. The latter has never been very well documented but it seems intuitively true whereas health hazards are easily documented. In a study of retired asbestos workers, for example, I found an all cause SMR of 123.8 while in a very large study we recently completed on workers producing man made mineral fibers we found the all cause SMR to be 102.0 based on 4986 deaths.

While historically employment does not directly select for or against cancer, in recent years I have noticed a tendency for employers to select against cigarette smoking, either directly or indirectly. Some time ago I visited a large refinery chemical complex at a time when they had been making a recruitment effort to fill 30 vacancies. The day I arrived they had over 300 applicants. It interested me as to how the personnel manager would select 30 from over 300. My discussions with him led me to believe that his final choice probably represented a selection of population likely to live a very long time. Some of his criteria included no history of drinking or legal problems, no history of divorces or family troubles, a history of stable employment prior to applying for the present position, and perhaps no history of cigarette smoking. My impression was that the workers chosen were nonsmokers, nondrinkers with very stable family lives.

Clearly the question of a healthy worker effect is not a simple one. In general, however, I feel where there is no occupational hazard I would expect the workforce to have an overall death rate about 80% of the death rate in an appropriate reference general population and I would expect the cancer SMR to be higher than the all cause SMR. If the overall SMR is close to 100 I suspect a problem. An analysis by date of hire sometimes helps. If I find WWII hires or hires during periods of labor shortages are contributing heavily to the overall SMR I may modify my feelings about the SMR.

I do not attempt any adjustment for the "healthy worker effect" for specific disease categories. This is probably because I have mainly been concerned with cancer excesses where the healthy worker effect is probably minimal. If the cancer SMR is very low I suspect I've missed some deaths, have encountered a population containing many nonsmokers, or have the wrong reference population. I've also considered beneficial effects of employment as for cotton textile workers exposed to endotoxins.

COMPONENTS AND MODIFIERS OF A HEALTHY WORKER EFFECT: EVIDENCE FROM THREE OCCUPATIONAL COHORTS, AND IMPLICATIONS FOR INDUSTRIAL COMPENSATION

by

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SUMMARY

The components and modifiers of the healthy worker effect have been examined using mortality data for three occupational cohorts, the employees of Atomic Energy of Canada Limited followed between 1950 and 1981, a ten-percent sample of the Canadian labour force followed between 1965 and 1979, and workers at the Eldorado Resources Limited Beaverlodge uranium mine followed between 1950 and 1980. Two important components have been identified in these cohorts, namely initial selection of healthy individuals, and continuing employment of healthy individuals. There is less evidence for a contribution from the existence of differential risk factors amongst employed individuals compared with the general population. The healthy worker effect is however substantially modified by time since employment, sex, age, specific cause of death, and specific occupation. It is concluded that because of this variation it is inappropriate to account for the healthy worker effect by a single parameter, and all of the above factors have to be taken into account in any appropriate analysis. The effect of the healthy worker bias on assessing the causality of any observed association, and attributing cause in an individual case is also discussed: when the only available comparison group for an occupational cohort is the general population, the healthy worker effect is unlikely to have any substantial influence upon the interpretation of either of these two components of the compensation decision process. This would be particularly true for cancer, and even more so for lung cancer, often a disease associated with industrial compensation cases.

INTRODUCTION

The healthy worker effect is the name given to the observation that cohort studies of individuals employed in some occupation or industry usually show that such individuals have a lower mortality than the general population, which includes individuals who are not currently employed for various reasons.[1] The phenomenon seems first to have been described by Ogle,[2] who suggested that initial selection for employment of healthy individuals, and continuing employment of those who remained healthy was responsible for the healthy worker effect. Reports of the results of occupational studies in which comparisons are made with the general population usually take cognizance of the healthy worker effect, but few attempts have been made to identify and quantify its components and modifiers. An exception to this is the report by Fox and Collier[3] of the healthy worker effect as seen in a cohort study of those employed

in the U.K. vinyl chloride industry, but their results are based on a relatively small total number of deaths, which limits the stability of their estimates. The healthy worker effect is important in attempting to assess the causality of any observed association for an occupational cohort based on comparison with the general population. Although various methods have been proposed for taking it into account, for example by adjusting standardized mortality ratios (SMRs) by a constant factor,[1] or by using proportionate mortality,[4] these solutions have considerable limitations.

This paper describes the healthy worker effect as seen in three occupational cohorts whose mortality has been ascertained using computerized record linkage to the Canadian National Mortality Database.[5] The cohorts consist of: 1) employees of Atomic Energy of Canada Limited, a Crown Corporation responsible for the research and development of the Canadian nuclear power programme, and related technologies, whose members in general show no marked excess of deaths from any particular cause;[6] 2) a 10 percent sample of the Canadian labour force consisting of 700,335 individuals whose occupations between 1965 and 1969 have been recorded;[7] and 3) males employed by Eldorado Resources Limited at their Beaverlodge Uranium Mine in northern Saskatchewan between 1948 and 1980, where exposure to radon decay products has led to a large excess of lung cancer.[8] These data have been used to examine and quantify the components and modifiers of the healthy worker effect, and the distinctive nature of each of the cohorts makes comparisons amongst them particularly informative. The findings are discussed with respect to implications in assessing the causality of any observed association in an occupational cohort, and in particular to the implications for attributing causation for an individual who develops a disease, and consequently is under consideration for compensation.

THE HEALTHY WORKER EFFECT: COMPONENTS AND MODIFIERS

One may postulate at least four potentially important components of the healthy worker effect. The first arises at the time of initial employment. Individuals who have a diagnosed disease such as chronic bronchitis may either be less willing themselves to seek employment, or alternatively may seek employment but are more likely to be rejected by a potential employer on the basis of their disease. The effect could also operate for diseases not yet diagnosed, but which could still make an individual feel less able to seek employment, though presumably the effect would be less than for specifically diagnosed conditions. The second possible component again would occur primarily at the time of initial employment and relates to risk factors for disease such as smoking. If the characteristics with respect to such risk factors of those who seek employment are different from the general population, subsequent mortality from those diseases associated with the risk factor would differ in the employed cohort compared to the general population. Both the above factors are of course confounding variables in the classic sense, the first relating to confounding by current disease status, the other to confounding by current risk factor status. The third potential component of the healthy worker effect arises from preferential continued employment of those who remain healthy, and the tendency of those who develop disease to leave employment. Thus, if

comparisons are made between those who remain in employment during the time period of observation, with the general population, their mortality would be lower by reason of those who have already left employment due to disease. This factor should not in general apply to studies in which mortality is determined for an entire occupational cohort, irrespective of whether or not they continue in employment. Finally, a fourth component could arise from differential diagnosis of the cause of death for an occupational cohort as compared with the general population. An intensive review of death certification, and/or clinical records for the cohort could serve to identify cases of disease which would not be identified from routine death certification on which population statistics are based. Again, this fourth component would only operate where such special surveys have been carried out and are probably the exception rather than the rule.

The effect of all of the above four components might be expected to be modified by a number of factors. If the initial selection component is important, one would expect that the effect would diminish considerably with time since initial employment, particularly if the mortality experience of those who subsequently leave employment is included. Since there will obviously be a strong correlation between time since employment and increasing age, it is also necessary to examine the effect of age at observation to determine whether any time since employment effect is independent of an age effect. In addition to time since employment and age, other obvious important modifiers of the effect could be sex, the specific cause of death, and the type of occupation. These components and modifiers are examined below with respect to the three occupational cohorts described.

THE OCCUPATIONAL COHORTS

Full details of the three occupational cohorts have been described previously.[6,7,8] Mortality results with respect to lung cancer for the uranium miners study,[8] and cancer mortality amongst males for the ten percent labour force study[7] have been published. All three studies use the same method of follow-up, namely by computerized record linkage to the Canadian National Mortality Database maintained by Statistics Canada. The latter contains in machine readable form all deaths occurring in Canada since 1950, together with those of Canadian residents occurring in the U.S. Date of death and underlying cause of death coded to the appropriate revision of the international classification of diseases is available, together with personal identifying information. Since no unique identification number is available on the database, it is searched using the corresponding identifying information from the cohort records. The searching process makes use of a probablistic weighting system for comparing the individual items of identifying information, and the statistical theory and computer system used have been described elsewhere.[9] Brief details of each of the cohorts are provided.

Atomic Energy of Canada Limited (AECL) Study: This cohort consists of 13,570 current and ex-employees of AECL known to be alive as of January 1, 1950 and constitutes 92.8% of those originally defined as eligible for the study. The majority of those not included were current employees who did not wish to participate in the study. Identifying

information for the cohort was assembled from company records and by means of questionnaires completed by current employees. Mortality follow-up has been carried out between 1950 and 1981, resulting in 882 deaths amongst males and 66 deaths amongst females. A total of 159,845 person-years of observation have been accumulated by the 10,034 males in the cohort, and 54,807 person-years by the 3,536 females. The interest in this cohort arises since a number of the subjects are classified as radiation workers with exposure to well monitored doses of low-level low-linear energy transfer radiation. Based on current radiation risk-estimates,[10] it is unlikely that any significant excess of radiation related deaths will be observed in this cohort, but it is being monitored to confirm the adequacy of those estimates.

Labour Force Survey (LFS) Study: This cohort consists of 700,335 members of the Canadian labour force, constituting approximately a ten-percent sample. The survey was carried out by Statistics Canada to compile employment statistics, and records are available for individuals with recorded occupation and industry between 1965 and 1971. Records for 1970 have been lost, and a different coding scheme was employed for the 1971 records which was not compatible with that used for 1965-69. Therefore, the present analysis is restricted to occupations as recorded between 1965 and 1969. The personal identifiers for this cohort were obtained from the master index file of social insurance numbers. The mortality of the cohort between 1965 and 1979 has been monitored as described above, and a total of 41,194 deaths amongst males and 7,365 deaths among females has been observed. Person-years of observation total 5,467,282 for the 415,201 males, and 2,805,141 for the 285,134 females in the cohort. The study is intended as a routine monitoring in order to detect associations between occupation and risk of death not previously reported, and to confirm associations reported from other studies.

Eldorado Resources Limited (ERL) Study: The cohort consists of 8,487 males employed at some time in the Beaverlodge uranium mine operated by Eldorado Resources Limited in northern Saskatchewan between 1948 and 1980, and known to be alive as of January 1, 1950. This constitutes 77.5% of those originally deemed eligible, the majority of those excluded being due to missing birth years. Identifying information was assembled from company records, and mortality has been determined between 1950 and 1980, resulting in 603 deaths. Too few females were employed for any meaningful analysis, and the person-years at risk for the males are 118,337. This cohort represents one of the largest series of uranium miners studied to date, and has provided valuable data on the relationship between exposure to radon decay products and risk of lung cancer, of which there is a substantial excess amongst the cohort.[8]

METHOD OF ANALYSIS

The observed number of deaths and the person-years at risk were calculated for each study categorized by age group (15-19, 20-24...80-84, 85+), sex and calendar-year at risk (1950-54, 55-59...75-81). Entry to the study was defined as occurring during first year of employment for the AECL and ERL studies, and during first year for which an occupation was recorded for the LFS study. Year of exit was defined as year of death for those who died, or else the end of the last calendar

year in which mortality ascertainment had been carried out (1979 for the LFS study, 1980 for the ERL study, and 1981 for AECL study). Six causes of death were analyzed: lung cancer (a disease frequently the subject of compensation awards), other cancers, circulatory diseases, chronic respiratory diseases (bronchitis and emphysema), accidents and all causes of death combined. The expected number of deaths for any particular analysis were computed from the age, sex and calendar-year specific death rates for the disease under consideration for the Canadian population, applied to the appropriate person-years at risk in the cohort. Standardized mortality ratios (SMR) were then computed as: 100-percent multiplied by the ratio of the observed number of deaths to the expected number of deaths. The individuals enrolled in the LFS study were classified by social class I-V on the basis of their recorded occupations. The occupations were grouped into social classes using a system very similar to that used in the decennial supplement to the U.K. Registrar General's reports on occupation,[11] slightly modified for Canadian occupation.[12] Individuals were placed in the social class corresponding to the highest value for any of their recorded occupations. Data are presented in three groups corresponding to social classes I and II (professional and managerial), social class III (other white collar) and social classes IV and V (blue collar). A small number of occupations could not satisfactorily be classified, so the total presented (Table 6) are slightly less than those for the other analyses.

RESULTS

Table 1 shows SMRs and the number of observed deaths for all causes of deaths combined by period of follow-up for the various cohorts for both males and females. Both the AECL study and LFS study show substantial healthy worker effects, which decrease with increasing time of follow-up. The effect is stronger for the AECL study than for the LFS study, presumably reflecting the fact that follow-up in the AECL study is from start of employment, whereas in the LFS study it is by time since observation started, which acts as a surrogate for time since first employment. In contrast, the ERL data do not show the healthy worker effect for all causes of death. Another noticeable feature from Table 1 is that the effect is stronger for females than for males in both the AECL and LFS studies.

The contribution of the several specific causes of death to the overall effect are examined in Table 2 for the AECL and LFS studies. In general, the specific causes show the same increasing effect with time under observation as do all causes of death (details not shown). The patterns of the effect on the various diseases are generally consistent, though the data for the female AECL cohort are sparse and consequently are difficult to draw inferences from. The healthy worker effect is less for lung cancer than for other cancers, and in turn this is less than for all causes of death. The effect for circulatory diseases is less than for all causes of death in the LFS cohort, but the opposite is true for the AECL male cohort. The effect for deaths from respiratory diseases is less than that for all causes for both male cohorts, but is greater than for all causes for females, although the AECL female data are based on a single death.

In order to see whether the healthy worker effect for the ERL data are masked by the presence of occupationally related excesses for certain causes of death, the data for ERL are examined by cause and time under observation in Table 3. There is evidence for a healthy worker effect for cancers other than lung, and for respiratory diseases, the latter however is based on small numbers. The excess of lung cancer due to radon decay products is well established,[8] and the excess of deaths from accidents is again well recognized in mining cohorts. The pattern for circulatory diseases appears to have no obvious explanation.

Table 4 presents data for all causes of death by period of follow-up and age at risk. For all studies, and for all age groups the general pattern of a decreasing healthy worker effect with increasing period of follow-up is seen. (The AECL female data are too few to contribute to this detailed analysis). However, although the strongest healthy worker effect is seen for the youngest age group for the AECL male data, the reverse is true for both males and females in the LFS study. Some of these observations, particularly for young ages and greatest length of follow-up, and old ages and shortest length of follow-up are inevitably based on small numbers.

Table 5 examines the evidence for a component of the healthy worker effect due to the preferential continued employment of those who are healthy, by examining all causes of mortality for the male AECL cohort by a period of follow-up, classified as to whether or not the individual continued to be employed by AECL. For the first ten years of follow-up both groups show a substantial and similar decease in mortality relative to the population, but after that time period those who leave employment have a mortality approximately 50 percent greater than those who remain in employment.

Finally, Table 6 examines the effect of social class by cause of death for the LFS study cohort. For males, the greatest reduction in mortality compared to the population is for social classes I and II, compared to social classes III, IV and V. Although the overall mortality for class IV and V is similar to that for class III, there are differences for the individual causes of death. In particular, lung cancer deaths are higher for classes IV and V, but their rate for other cancers is lower. Classes IV and V also have lower rates from circulatory diseases, but substantially increased rates from accidents. For females, the differences between the social classes in general appear somewhat less than for males as judged by overall mortality. However, again lung cancer is increased in social classes IV and V, as are accidents compared to the other social classes.

DISCUSSION

Empirical Evidence for Components and Modifiers of the Healthy Worker Effect: The results reported in the previous section come from three very different cohorts. The LFS study represents a 10-percent sample of the entire Canadian labour force, and thus represents a diverse collection of occupations and industries. The AECL cohort represents an occupational group in which a priori one would expect no large excesses from any particular cause of death, and probably represents a higher than average social class group, containing many skilled white and blue

collar workers. In contrast, the ERL study consists primarily of uranium miners, many of whom are non-skilled. They have expected high rates of mortality from lung cancer due to exposure to radon decay products, and from industrial accidents. The data confirm the importance of at least two components of the healthy worker effect, namely the initial selection process, and the continuing employment component. (Tables 1 and 5 respectively). However, the healthy worker effect is subject to substantial modification by time since employment, sex, specific causes of death, age, and type of job. In general, the maximal effect is observed during the first five years of employment, and has almost disappeared 20 years after first employment for the AECL males, or in the case of the LFS study, 10 years after first observation. The only exception are female AECL employees, which although based on small numbers still shows a substantial reduction in overall mortality compared to the population 20 years after first employment. It is clearly demonstrated in both AECL and LFS studies that the effect is stronger for females than males, and this appears consistent for the individual causes of death considered. The general pattern of a decreased effect for lung cancer and a smaller decreased effect for other cancers is not unexpected: cancer has a high fatality rate, particularly lung cancer, and consequently the initial selection bias disappears more rapidly for cancer than for other long term chronic diseases such as cardiovascular disease. The effect of age as seen in the LFS data is consistent with that observed by Fox and Collier for the U.K. vinyl chloride workers,[3] but seems to operate in the opposite direction for the AECL cohort. There is no obvious reason for this difference, but it is marked and presumably represents different selection criteria for different industries which operate differentially at different ages.

The evidence supporting a role for confounding by risk factors as a component of the healthy worker effect is much less striking. As stated, the cohorts in general achieve the mortality of the population after a number of years under observation. The social class data shown in Table 6 do indicate that occupations in the higher social classes (I and II) do have a persistent lower mortality than the general population, as compared to other social classes both white collar and blue collar. However, the data in Table 6 again illustrate the necessity of considering factors such as specific cause of death, since this clearly indicates that there is a differential between class III and classes IV and V with respect to diseases such as lung cancer, presumably reflecting differences in smoking habits.

In summary the study has demonstrated strong evidence for two components of a healthy worker effect, namely initial selection and continuing employment, but suggests that a component resulting from confounding by risk factors makes much less contribution to overall mortality, though it may play a role in certain specific diseases. A number of factors modify the healthy worker effect, and consequently it is not possible to make generalizations about a single "healthy worker effect", and in particular the suggestion of correcting for such an effect using a single figure as proposed for example by Goldsmith[1] would not be valid, and could indeed be very misleading.

Implications for Industrial Compensation: In assessing the relevance of the healthy worker effect to the issue of industrial compensation it is necessary to consider the effect on two parts of the compensation decision process. These are 1) the decision that an observed association between occupational exposure and risk of disease is causal and 2) the model used for attributing causation in a particular individual case. The third part of the process, namely the model used for compensation is often a subjective process, and subject to wide variation in various jurisdictions and cannot realistically be considered here.

In assessing the causal nature of any observed association it is traditional to consider a number of criteria.[13] The two criteria primarily affected by the healthy worker effect are the observed strength of the association as measured by the relative risk and the statistical significance of the association. These two factors relate to possible contribution by systematic error and random error respectively to the observed association. If no appropriate internal control group is available (see below) and the relative risk is estimated by the SMR comparing the occupational cohort to a general population, the healthy worker effect will generally tend to bias the estimated relative risk towards unity, although the magnitude of this bias will vary as discussed above with time since employment, age, sex, cause of death and type of occupation. This therefore will weaken any conclusion as to causality based on the strength of association. However, the reduction in the strength of the evidence will be most marked when the true value of the relative risk is small, and when the bias is large. For example, if the bias (B) is defined as:

$$B = \frac{R(u,z)/R(p,z)}{R(e,z)/R(p,z)} = \frac{R(e,z)/R(p,z)}{R(e,z)/R(u,z)} \qquad (1)$$

$$= \frac{\text{Obs. RR}}{\text{True RR}}$$

Where R(e,z) is the risk of disease of an individual with a vector of exposure variables (e), and a vector of covariates (z), R(u,z) is the risk for an individual without exposure and with a set of covariates (z), and R(p,z) is the risk for an individual in the comparison population with the same set of covariates. If the value of B is 0.8, which represents a fairly typical healthy worker effect, and the true relative risk is 2.0, the observed relative risk on average will be 1.6, whereas if the true relative risk is 5, on average the observed relative risk would be 4. In the former case it would appear more likely that the observed association could be due to confounding, than in the latter case. However, when considering the significance of any observed association, it is conceivable that using comparisons with the general population can increase the power in relation to a comparison with an internal control group, despite the healthy worker effect. For a given number of observed deaths in the exposed group, the increase in power will be greater as the true relative risk increases, and as the bias from the healthy worker effect decreases.

In order to assess the effect of the healthy worker effect on the attribution of causality in any individual case it is necessary to develop the appropriate model for attribution. The probability that an observed death arises from exposure will be given by:

$$PC = \frac{R(e,Z)-R(u,z)}{R(e,z)} \qquad (2)$$

assuming that the difference in risks arises solely because of a causal relationship between exposure and disease. Obviously, this probability of causation as expressed in equation 2 will be a function of the underlying risk for the individual i.e. will be specific for a particular set of covariates (z) and any interaction with the exposure factor (e). It is therefore necessary as usual to assume some form of probabilistic model in order to come up with stable estimates of the probability of causation. The usual model chosen is the multiplicative one i.e.:

$$PC = \frac{RR(e)-1}{RR(e)} \qquad (3)$$

derived from equation 2 above by assuming that the relative risk is a function only of the exposure vector and is independent of the covariates. The empirical evidence for the multiplicative model has been discussed extensively[14] and although it is generally difficult to definitively determine the nature of the relationship between risk from exposure to occupational factors, and risk from other factors, the multiplicative model is frequently chosen. If a bias is introduced into the relative risk estimation by the healthy worker effect, the bias (B') introduced in the probability of causation under the multiplicative model is given by:

$$B' = \frac{RR(e)-1/B}{RR(e)-1} \qquad (4)$$

if B is less than unity as is generally the case, the bias in the probability of causation will also be less than unity i.e. the observed probability of causation will be less than the true probability of causation. Table 7 shows some examples of the bias in the probability of causation as a function of the true relative risk and the bias in the relative risk due to the healthy worker effect. The bias in the PC decreases as the relative risk increases, and as the bias from the healthy worker effect decreases, but is often substantially less than the bias in the relative risk itself. In fact, the bias in the PC will be less than the bias in the relative risk provided that:

$$RR = \frac{1/B-B}{1-B} \qquad (5)$$

thus if the bias in the relative risk is 0.5, any true relative risk greater than 3.0 will show a reduced bias in the PC, and a bias of 0.8 in the relative risk estimate will result in a smaller bias in the PC for any true relative risk greater than 2.25.

CONCLUSION

In analyzing the results of any occupational cohort study estimates of risk, both for assessing causality, and for use in an attribution of causation model, are best based on internal comparisons, in order to minimize bias due to the healthy worker effect. However, this will only be true when an appropriate internal comparison group exists i.e. one of sufficient size to yield adequate power, and one which is either comparable to the exposed group in terms of potential confounding variables, or has measures of those variables which can be controlled in analysis. It will also generally be sensible to present results compared to general population rates, even when these are not used for definitive risk estimation. It is also apparent from the results presented in this paper, that for an internal analysis, it is necessary to take account of factors such as time since first employment, and continued employment, if these factors differ among the exposed and non-exposed members of the cohort.

When an appropriate internal control group is not available, the use of general population rates (specific for age, sex, race, location and calendar year) provides a sensible alternative for risk assessment, despite the healthy worker effect. The use of such a comparison will generally increase the power of any study despite the downward bias generally introduced by the healthy worker effect, and this is particularly true as the relative risk increases and as the bias decreases. In addition, for reasonably large relative risks, and the order of the bias generally seen, the healthy worker effect is unlikely to make a substantial difference to the assessment of causality as based on the strength of the association. If a model for the probability of causation is used to attribute cause in an individual case, the bias in the probability of causation is likely to be less than the bias in the relative risk estimate itself, and this reduction in the bias will increase as the relative risk increases, and as the healthy worker effect bias decreases. Many of the associations recognized for industrial compensation involve cancer as an outcome. The healthy worker effect in general appears smaller for cancer than other causes of death. In addition, the attribution model often specifies a minimum latent period typically of ten years. The latent period generally is highly correlated with time since first employment, again this tends to minimize the bias due to the healthy worker effect. Thus, for these particular situations it is likely that any bias introduced by the healthy worker effect when using population rates for comparison will be minimal, and the bias in the probability of causation will be even smaller and thus negligible.

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TABLE 1
SMRs AND OBSERVED NUMBER OF DEATHS FOR ALL CAUSES OF DEATH
EFFECT OF PERIOD OF FOLLOW-UP

Period of follow-up (years)*	Study				
	AECL		LFS	ERL	
	males	females	males	females	males
0-4	54.1 (61)	19.6 (3)	74.4 (77.65)	59.3 (1149)	130 (106)
5-9	58.7 (84)	36.0 (6)	85.4 (14573)	71.4 (2436)	103 (96)
10-14	82.9 (140)	37.7 (7)	108 (18856)	100 (3780)	102 (116)
15-19	85.3 (157)	58.7 (12)	-	-	108 (132)
20-24	95.4 (187)	70.3 (15)	-	-	97.3 (114)
25+	96.6 (253)	72.3 (23)	-	-	73.3 (39)
TOTAL	82.7 (882)	53.2 (66)	90.7 (41194)	78.6 (7365)	104 (603)

* Time since first employment for AECL and ERL studies, since 1965 for LFS study.

TABLE 2

SMRs AND OBSERVED NUMBER OF DEATHS

EFFECT OF CAUSE OF DEATH

Cause of death	Study			
	AECL		LFS	
	males	females	males	females
Lung Cancer	102 (68)	0* (0)	107 (3254)	112 (283)
Other Cancers	83.4 (131)	82.0 (31)	94.3 (6485)	89.1 (2482)
Circulatory diseases	94.3 (436)	31.4 (11)	87.4 (17826)	69.1 (2261)
Respiratory diseases	73.0 (14)	108.5 (1)	81.9 (872)	80.9 (69)
Accidents	56.7 (72)	49.8 (6)	103 (4686)	94.0 (669)
All Causes	82.7 (882)	53.2 (66)	90.7 (41194)	78.6 (7365)

* Expected number of deaths = 3.41

TABLE 3

SMRs AND OBSERVED NUMBER OF DEATHS

EFFECT OF PERIOD OF FOLLOW-UP BY CAUSE OF DEATH FOR ERL MALES

Period of follow-up (years)*	Cause of Death					
	Lung Cancer	Other Cancers	Circulatory Diseases	Respiratory Diseases	Accidents	All Causes
0-9	190 (11)	67.8 (14)	72.5 (38)	0 (0)	189 (97)	115 (202)
10-19	225 (33)	81.2 (28)	70.7 (70)	23.2 (1)	186 (59)	105 (248)
≥20	153 (21)	88.2 (24)	51.7 (40)	165 (6)	174 (20)	89.8 (153)
TOTAL	190 (65)	80.2 (66)	64.7 (148)	74.5 (7)	186 (176)	104 (603)

* Time since first employment for LFS study.

TABLE 4

SMRs AND OBSERVED NUMBER OF DEATHS FOR ALL CAUSES OF DEATH

EFFECT OF AGE AND PERIOD OF FOLLOW-UP

Age at risk	Period of follow-up* (years)	Study			
		AECL	LFS		ERL
		Males	Males	Females	Males
15-39	1	45.9 (43)	85.5 (1349)	70.0 (261)	139 (114)
	2	80.2 (28)	92.1 (1681)	82.9 (396)	103 (34)
	3	114 (1)	132 (1450)	134 (438)	0 (0)
	TOTAL	55.6 (72)	103 (4480)	95.2 (1095)	129 (148)
40-64	1	59.2 (86)	76.6 (4507)	59.5 (723)	93.8 (80)
	2	80.6 (187)	89.8 (7342)	71.2 (1379)	111 (168)
	3	90.8 (226)	117 (8258)	104 (1387)	105 (106)
	TOTAL	79.7 (499)	95.4 (20107)	79.4 (3939)	105 (354)
>65	1	95.1 (16)	64.1 (1909)	47.3 (165)	104 (8)
	2	95.2 (82)	78.6 (5550)	66.4 (661)	88.9 (46)
	3	102 (213)	98.7 (9148)	89.9 (1505)	68.1 (47)
	TOTAL	99.9 (311)	83.2 (16607)	71.7 (2331)	78.6 (101)

* Period of follow-up for AECL and ERL study, 1 = 0-9 years; 2 = 10 - 19 years; and 3 = 20+ years.
Period of follow-up for LFS study, 1 = 1965-69; 2 = 1970 - 74; and 3 = 1975 - 79.

TABLE 5

SMRs AND OBSERVED NUMBER OF DEATHS FOR ALL CAUSES OF DEATH

EFFECT ON CONTINUING EMPLOYMENT FOR AECL STUDY (MALES)

Period of follow-up (Years)*	Currently Employed	No Longer Employed
0 - 9	59.6 (52)	55.1 (93)
10 - 19	61.3 (48)	90.7 (249)
≥20	62.9 (36)	101 (404)
TOTAL	61.0 (136)	88.4 (746)

* Time since first employment

TABLE 6

SMRs AND OBSERVED NUMBER OF DEATHS

EFFECT OF SOCIAL CLASS AND CAUSE OF DEATH FOR LFS STUDY

	Social Classes					
	Males			Females		
Cause of death	I - II	III	IV - V	I - II	III	IV - V
Lung	82.1 (266)	98.6 (472)	112 (2494)	92.2 (19)	107 (136)	122 (128)
Other Cancers	92.3 (671)	101 (1106)	93.2 (4677)	92.9 (206)	89.4 (1253)	87.5 (1004)
Circulatory Disease	82.5 (1768)	96.5 (3120)	86.1 (12823)	63.1 (176)	66.2 (1058)	73.7 (1015)
Respiratory Diseases	56.0 (61)	80.3 (135)	85.8 (671)	113 (8)	63.9 (27)	95.6 (34)
Accidents	58.6 (292)	65.3 (519)	120 (3835)	92.5 (41)	86.5 (334)	104 (286)
All causes	77.7 (3739)	91.0 (6653)	92.5 (30522)	75.2 (559)	76.7 (3608)	81.5 (3146)

TABLE 7

BIAS IN PROBABILITY OF CAUSATION (PC)*

AS A FUNCTION OF

TRUE RELATIVE RISK (RR) AND BIAS IN RELATIVE RISK (B)

		B		
RR	PC	.7	.8	.9
2.0	50	.57	.75	.89
4.0	75	.86	.92	.96
8.0	88	.94	.96	.98

* $PC = \frac{\text{Observed Probability of Causation}}{\text{True Probability of Causation}}$

ASSIGNING HANDICAPS IN THE MORTALITY STAKES: AN EVALUATION OF THE "HEALTHY WORKER EFFECT"

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DEFINITION OF HWE

The phrase "Healthy Worker Effect", frequently referred to in the interpretation of occupational epidemiological studies, is easily misinterpreted. The "Healthy Worker Effect" (HWE) refers to the consistent tendency for actively employed people to have a more favorable mortality experience than the population at large. Despite the clarity seemingly implicit in its name, the HWE is not an intentional measurement of the relative good health of a working population; nor does it quantify the beneficial effects of the occupational environment upon those working within it. Rather, it is an unintended bias, of uncertain magnitude, in an unavoidably imperfect comparative measure of the health status of a working population.

Such imperfect comparison occurs whenever a population of workers, exposed to some occupational factor of research interest, is compared, not with some other equivalent population of unexposed workers, but with the general population. Such an "external" comparison is typically made when the whole membership of some particular workforce is thought to be at altered risk of some health outcome. If just one group of workers within such a workforce is thought to be at increased risk (because of some localized occupational exposure), then the logical thing to do is to compare "internally" the exposed group with the residual unexposed group. However, such an internal comparison requires that, at some level, satisfactory exposure data exist that enable distinctions to be made between individual (or at least, groups of) workers.

In comparing the health of a working population with the health of the general population, the HWE is that component which biases the comparative measure downwards because of between-population differences in health status which are unrelated to occupational exposure, and which independently influence the health outcome under investigation.

ROLE OF COMPARISON IN EPIDEMIOLOGY

The basic research strategy of epidemiology (and indeed of most sciences) is comparison. To ascertain the strength of a "causal" relationship, epidemiologists determine the relative risk (or relative probability) of the occurrence of some specified health outcome in two

compared populations known to differ in their experience of some putative "risk factor". This comparison is typically non-experimental, or observational, and entails no intervention within the study population.

Ideally, the two populations selected for comparison would differ only in their experience of this factor, and any observed difference in the subsequent occurrence of the specified health outcome could therefore be attributed to the factor. In reality, the two populations will differ in other ways that influence the occurrence of the health outcome-mostly actual differences in exposure to risk factors, but perhaps also in quality of measurement of health outcome. The comparison will therefore be biased.

The general methodological challenge to the epidemiologist is to anticipate the sources of such bias, and then to either minimize them in the study design, or to adjust for them in the data analysis. However, it is in the very nature of the HWE that, by definition, it is difficult to reduce this "effect" when comparing the health of an active working population with that of the general population. While it is not possible to quantify the HWE with any precision within a single study, it tends typically to bias the relative risk of mortality within industrial working populations downwards by approximately 10-30% below the null value (McMichael, 1976; Wen et al., 1983).

NATURE OF EFFECT

If we assume that the occupational environment per_se has no effect on the health of the working population under study, then the HWE is the manifestation of the other non-occupational influences that confer actual, or apparent, health advantage on the working population relative to the general population. Those influences are as follows:

Bias

Bias refers to any systematic tendency of a study to misrepresent the true relationship of interest within the source population (i.e. the population from which the study population derives). It usually arises from two major sources:

1) non-random sampling of one or both of the compared populations (i.e. selection bias); or

2) differences in the quality of the information collected about/from the two compared populations (i.e. classification bias).

Selection bias

Selection of individuals into the working population is the major, and best-known source of the HWE. On average, persons healthy enough to be initially employed, and to subsequently stay employed, are in better

health than the average person within the general population. The general population contains many unfit, unwell, or institutionalized persons, not able to obtain or keep employment, and who have poorer health prospects than their employed peers. Studies in the US and Finland have documented a greater than twofold increase in mortality in occupationally inactive men compared to the general population (Kitagawa and Hauser, 1973; Sauli, 1979).

Selection bias, in general, is construed to mean that the method of selection of the study population is such that it will misrepresent the true relationship of interest within the source population. However, in the case of the HWE, the problem is best thought of not as one resulting from the preferential selection of healthy individuals into the workforce, but instead as one in which the theoretical source population is not known. The correct comparison population for a particular population of actively employed persons is the remainder of the immediate underlying source population - which, notionally, comprises all other persons of equivalent health status who could have entered that particular workforce but who did not.

Clearly, the general population has a different composition and a different health status from that theoretically correct comparison population.

A subsequent element of selection bias can occur if those workers leaving (voluntarily or through termination) the workforce are of different health status to those who remain and if follow-up of the out-migrating section of the cohort is incomplete. Fox and Collier (1976) found among British chemical workers that the terminated group had a more adverse mortality experience than did the non-terminating workers.

Classification bias

In any such external comparison, the methods and quality of recording of health outcome may well differ between the two compared populations. Thus, in the absence of a difference in rates of total mortality or of total hospital morbidity between the working population of interest and the general population, there might still be differences in rates of specific categories of outcome because of differences in the diagnostic criteria, in expectations of certain outcomes, or in the standards of data recording being applied to these two different populations. Shindell et al., (1978) questioned whether the HWE may not sometimes be artifact rather than fact, as a result of under-ascertainment of death or disease in the working population.

Confounding

Whereas the selection bias discussed above depends on differences in background health status between the two compared populations, confounding depends on inter-population differences in other risk factors. These risk factors influence the probability of the health outcome being studied, and might include such things as smoking, alcohol

consumption, dietary habits, recreational exposure to noxious substances, and previous occupational exposures.

In occupational epidemiology, the most informative comparison will be that in which there is a substantial difference between the compared groups of workers in their exposure to the factor of interest (e.g. solvent fumes), while they differ little in other background factors that also influence the health outcome under investigation. In other words, one seeks a balance between maximizing the inter-population difference in exposure, while minimizing confounding. That principle is illustrated in **Figure 1**, wherein the comparison is between two groups of workers with job exposures A and non-A, selected because they differ little in their exposure to extraneous factors (or because one can measure and then adjust for such factors). This approach can be thought of as raising the signal-to-noise ratio of the comparison.

If employers intentionally recruit individuals with lower levels of such risk factors, then the unequally distributed effect of those factors upon the health outcome will confound the study of the relationship of the occupational exposure of interest to that same health outcome. It is also likely that some occupational environments will confer health benefits on active employees, associated, for example, with enhanced income, health insurance, and provision of health promoting facilities and advice at work.

EXAMPLES

General remarks

Mortality statistics are routinely compiled for the general population, based on the statutory registration of deaths and on the periodic population census. Morbidity statistics are usually not available on a systematic basis for the whole population. Hence, most comparisons of the health of working populations with the general population have been comparisons of mortality.

The comparative measure of mortality, the "relative risk", is the ratio of the death rate in the working population to the death rate in the general population. In calculating this ratio, it is usual to adjust (control) for differences in basic confounders: age, sex, and, where appropriate, race. The Standardized Mortality Ratio (SMR) is a widely-used confounder-adjusted relative risk of mortality. The null value of the SMR is 100, at which value the death rates in the two compared populations are equal.

During the 1970s, as the tempo of occupational epidemiological research increased, it became clear that the SMR for overall mortality in actively employed populations, compared with the general population, was frequently below 100. Assuming equal quality of recording of mortality

in the two compared populations, the three main competing explanations for this apparent mortality deficit were:

1) Working within that particular occupational environment was beneficial to health - more specifically, to longevity.

2) The individuals within that particular working population came from a socioeconomic or subcultural background of below-average risk of mortality.

3) The comparison was biased, because individuals entering and staying within the active workforce have better-than-average underlying health status.

The first two explanations were manifestly improbable for many of the working populations studied. These populations were, typically, industrial workforces from low socioeconomic status backgrounds working in occupational environments in which exposures to hazardous chemical and physical agents were common.

Yet it was not unusual to observe, for those industrial cohorts of workers, all-causes SMR's within the region of 70 to 90 - compared to an expected (or null) value of 100. Therefore, attention was directed principally to the third of the above explanations in seeking to explain this phenomenon called the "healthy worker effect" (McMichael, 1976; Fox and Collier, 1976).

Nevertheless, it should be remembered that the HWE is necessarily an imprecise and multifaceted concept, and that it takes on different content and magnitude in different settings. For example, in comparing the mortality experience of a white-collar or clerical workforce to that of the general population, the mortality deficit is as likely to be due to socioeconomic confounding (i.e. explanation 2 above) as to selection bias (explanation 3).

All-causes Mortality

Rubber workers (McMichael et al., 1974)

In our cohort study of approximately 7,000 male rubber workers in the US, followed for 10 years, the all-causes SMR for workers aged 40-64 years was 87 (McMichael et al., 1974). The magnitude of the HWE was inversely related to age, as shown in **Figure 2**. Beyond age 75 (i.e. 10 years into retirement, and with no selective forces any longer operating), the mortality advantage had totally dissipated. This general age-related pattern has been reported in other industrial cohorts (see also McMichael, 1976).

Other cohorts

Tola and Hernberg (1983) have given examples of various other industrial cohorts with all-causes SMR's clearly below 100: vinyl chloride workers, steel foundry workers, granite workers, dock workers, carpenters, and chemical workers. In each case, the mortality comparison was with the general population.

An ongoing cohort study of approximately 10,000 male petroleum industry workers in Australia, aged 20-79, has reported an all-causes SMR of 65 (Christie et al., 1987). This figure, based on the conventional comparison with the general male population, increased to 86 when the comparison was made with the population of male contributors to the national government's superannuation scheme - i.e. with other men who were actively employed (in this case, by the national government).

CAUSE-SPECIFIC MORTALITY

A frequent finding is that the SMR for ischaemic heart disease (the major cause of death in Western populations) is a little lower than the all-causes SMR. By contrast, the all-cancers SMR tends to be closer to the null value of 100. (See, for example, **Figure 3**, based on Milham, 1974).

In our rubber worker cohort, the SMR's for ischaemic heart disease and cancer were 99 and 103, respectively (McMichael et al., 1974). In the Australian petroleum industry workers cohort, the ischaemic heart disease SMR is 70, while the all-cancers SMR is 91 (Christie et al., 1987).

It is likely that this pattern reflects the variable extent to which the risk factors for specific diseases can be addressed in the selection processes by which individuals enter and remain in the workforce. For example, individuals who are obese and who have high blood pressure are readily identified, and their selective exclusion from the workforce would tend to enhance the reduced risk of cardiovascular disease in actively employed persons. On the other hand, cigarette smoking, the major risk factor for cancer in men, has not in past years been a criterion for recruitment or retention of employees.

Also relevant is the fact that while some conditions, such as coronary heart disease and diabetes mellitus, entail recognizable chronic clinical courses, some other diseases (including cancer) have a typically "silent" course until their later stages. Thus, cancers occurring within several years of entry into a workforce could not usually have been predicted at recruitment, whereas cardiovascular diseases often could have.

One important implication of this variation in the HWE across specific causes of death is that the use of proportional mortality analysis

(Kupper et al., 1978) does not provide a means of controlling for the HWE. If all the specific causes of deaths were equally affected by the HWE, then - in the absence of disease-specific risk factors - the proportions of all deaths caused by any one specific cause of death would be constant, irrespective of the magnitude of the HWE. Against that expectation, a shift in the proportion of deaths accounted for by that specific cause of death would then constitute evidence of an occupational exposure increasing the risk of occurrence of that specific disease.

MODIFIERS OF THE HWE

From the above, it is clear that the HWE is not a "constant". Rather, it varies between studies, depending on choice of comparison population and on the underlying strength of selection bias. Further, within a single study population it varies between different categories of workers and different causes of disease and death.

The most basic and constant modifier is age, as demonstrated above. Not only does age tend to be a surrogate measure for time since selective entry into the workforce, but at young ages the actively employed workers are being compared with age categories within the general population within which mortality is comparatively high from conditions that keep some individuals out of the workforce (including congenital diseases and disabilities, and personality and behavioural disorders).

Another modifier, closely related to age, is time elapsed since entry into the workforce: the greater the elapsed time the less the magnitude of the HWE (McMichael, 1976; Wen et al., 1983). The variation in the HWE associated with elapsed time will depend on the absolute strength of the initial selection process into the workforce, and on its magnitude relative to that of any subsequent selective removal of less healthy individuals from the workforce. An analogous process of attrition of initial health advantage occurs in some immigrant populations; within about five years of migration markedly lower mortality begins to move strongly up towards that of the host population (McMichael and Giles, in press). Migration, like entry and retention into the workforce, involves some strong health-related selection processes - both self-selection and externally imposed selection.

The socioeconomic status of the working population, or its subcultural background, will influence its underlying general health status and risk of death. White-collar workers will tend to have lower SMR's than blue-collar workers when each is compared to the general population. This represents more a reflection of conventional confounding (due to the unequal distribution of other separate risk factors), rather than being a consequence of active health-related selection of individuals.

DISCUSSION

Inferences about the HWE

As indicated at the outset, the Healthy Worker Effect is not a precise and simple entity. It is an inconstant and multi-faceted effect, reflecting deficiencies in the choice of an external comparison population and, perhaps, an attendant element of variability in the quality of data about the health outcome of interest (usually death).

For cancer mortality, the HWE appears to be of less magnitude than for most other major categories of cause of death. Since studies of occupational cancer are usually concentrating on one or a few specific types of cancer, it may be reasonable to take as the null value the all-cancers SMR or the value of 100 - which ever is the lower.

Options for minimizing or adjusting for the HWE

The essential first consideration in seeking to avoid or minimize the HWE is to identify the theoretically correct external comparison population - or a representative sample of it. This ideal external reference population comprises all other actively employed persons who have entered and remained in the workforce via equivalent selective processes.

Since such a population does not exist on any accessible register, the problem then becomes one of making a professional judgement about which of the available study populations would afford the least biased and the least confounded comparison. (The example above, from the Australian petroleum industry cohort, demonstrates well the substantial increase in SMR's - taken to illustrate a substantial reduction in the HWE - that results from use of an actively employed workforce as comparison population.)

The biasing effect of health-related selection into the workforce can be reduced by restricting the analysis of the health experience of the working population to that occurring after some minimum specified time since commencement of employment - eg. five years. A further adjustment for the HWE may be achieved by tracing and including those individuals who leave the workforce before retirement - since some such quitting of employment will be related to adverse health status.

Since the magnitude of the HWE varies between settings, and since its magnitude in any one setting is actually unknowable, it is not appropriate to apply a standard correction factor, such as was originally proposed by Goldsmith (1975). Further, for the reasons discussed above, the use of proportional mortality analysis does not remove the problem of the HWE, since the HWE affects different causes of death to differing, and - within any one study - unknown, extents.

The best solution to the problem of the HWE is to progress from external comparisons to internal comparisons. There are very few working

populations for whom the most important question is: Does this industry overall increase the risk of serious disease or death? More often we want to know if some exposed subgroup of workers has a different health experience from the other, unexposed, workers. Or we may want to examine the variation in health outcome rate across a gradient of increasing exposure within that workforce.

These latter two categories of questions can be better answered as industry becomes better at collecting and storing information on, first, the detailed job histories of employees, and, second, the characteristics of the occupational environment. With the development of more systematic occupational hygiene measurements (including biological monitoring), and the associated development of job-exposure matrices (Hoar, 1981), the assigning of estimated exposures to individual workers becomes more possible.

Indeed, with the growing emphasis on setting exposure standards in relation to exposures that are relatively low, and which are likely to be associated with relatively small adverse effects on health, it is becoming imperative that detailed and rigorous internal comparisons be made. The recent controversy in the US over the acceptable level of occupational exposure to benzene (McMichael, 1987) is now being resolved by the appearance of data based on internal comparisons across the range of cumulative exposures (Rinsky et al., 1987).

CONCLUSION

In conclusion, the Healthy Worker Effect is an empirically observable phenomenon within those occupational epidemiological studies that compare the health experience of a whole working population with that of the population at large. Since, in addition to selection bias, the HWE may also be contributed to by classification bias and by confounding, and since the net effect of the specific occupational environment upon health is not separately measurable, it is not possible to quantify the HWE. Further, since it varies by an unknowable amount for different diseases and causes of death, it is not possible either to correct for it, or to preclude it by using proportional mortality analysis.

The immediate solution is to identify, if possible, a more appropriate external comparison population. However, if - as is usually the case- the occupational exposure of research interest is not spread evenly throughout the working population, then a more informative aetiological analysis will result from internal comparisons of subgroups within that working population. In general, intra-population comparisons provide much more detailed and precise information about the aetiology of occupational diseases and disorders - while at the same time avoiding the problem of the Healthy Worker Effect.

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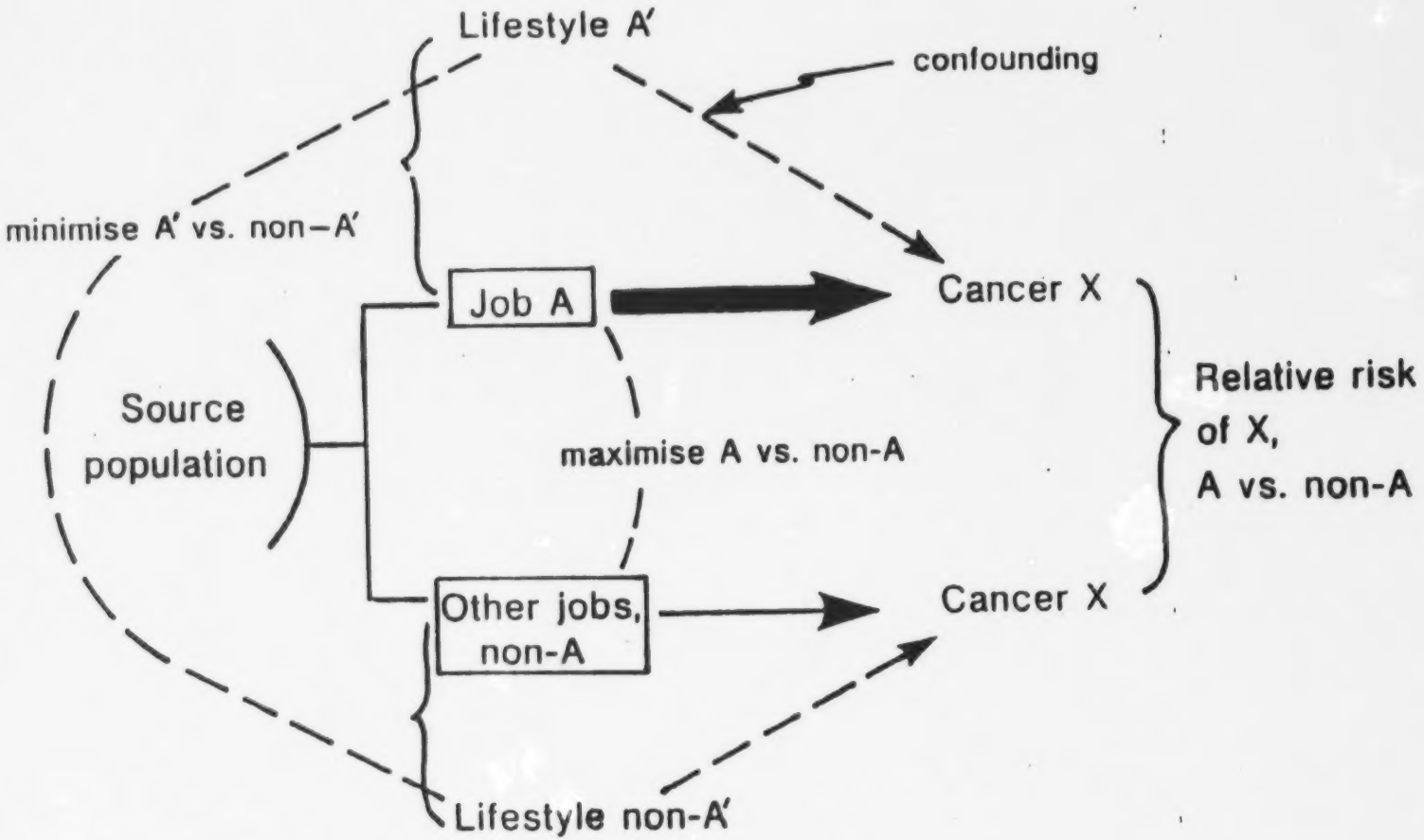
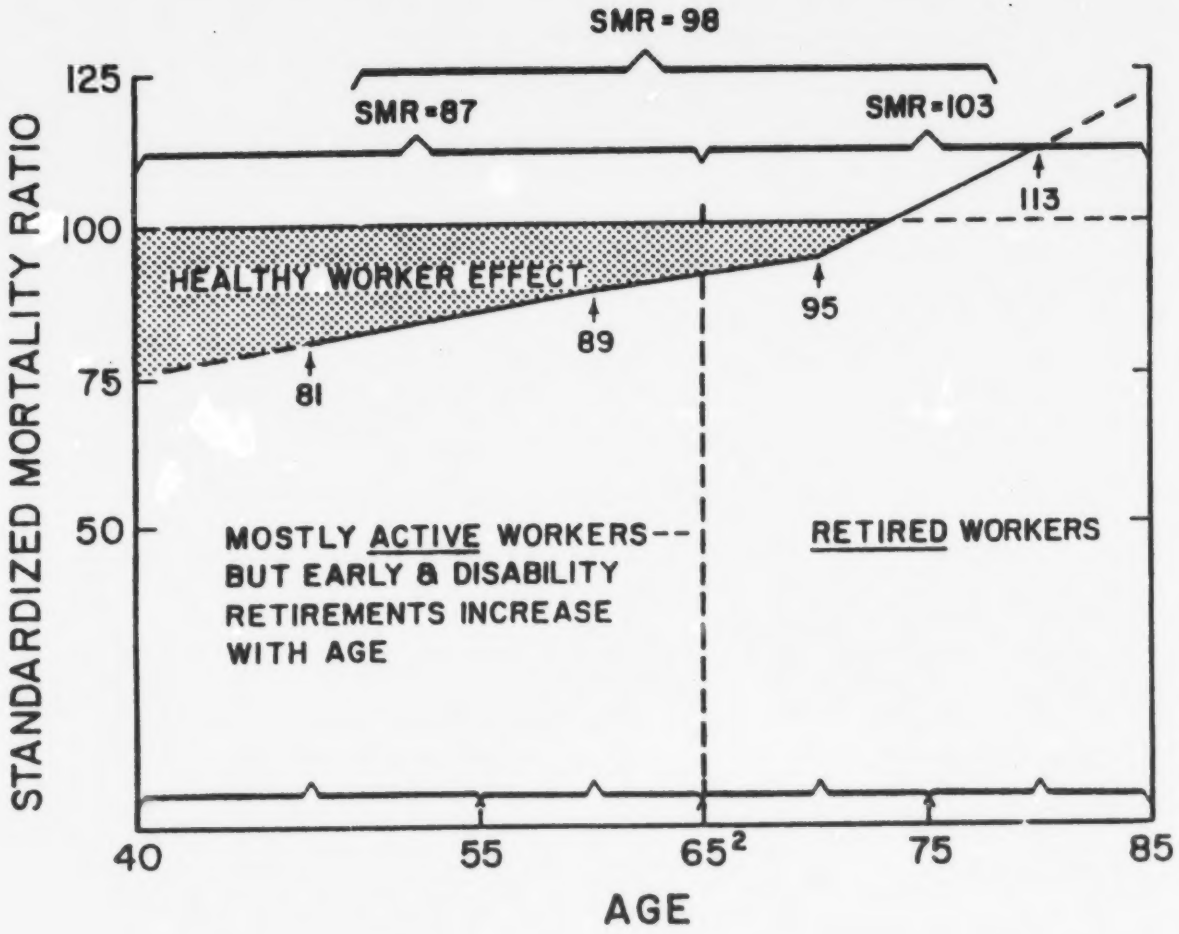
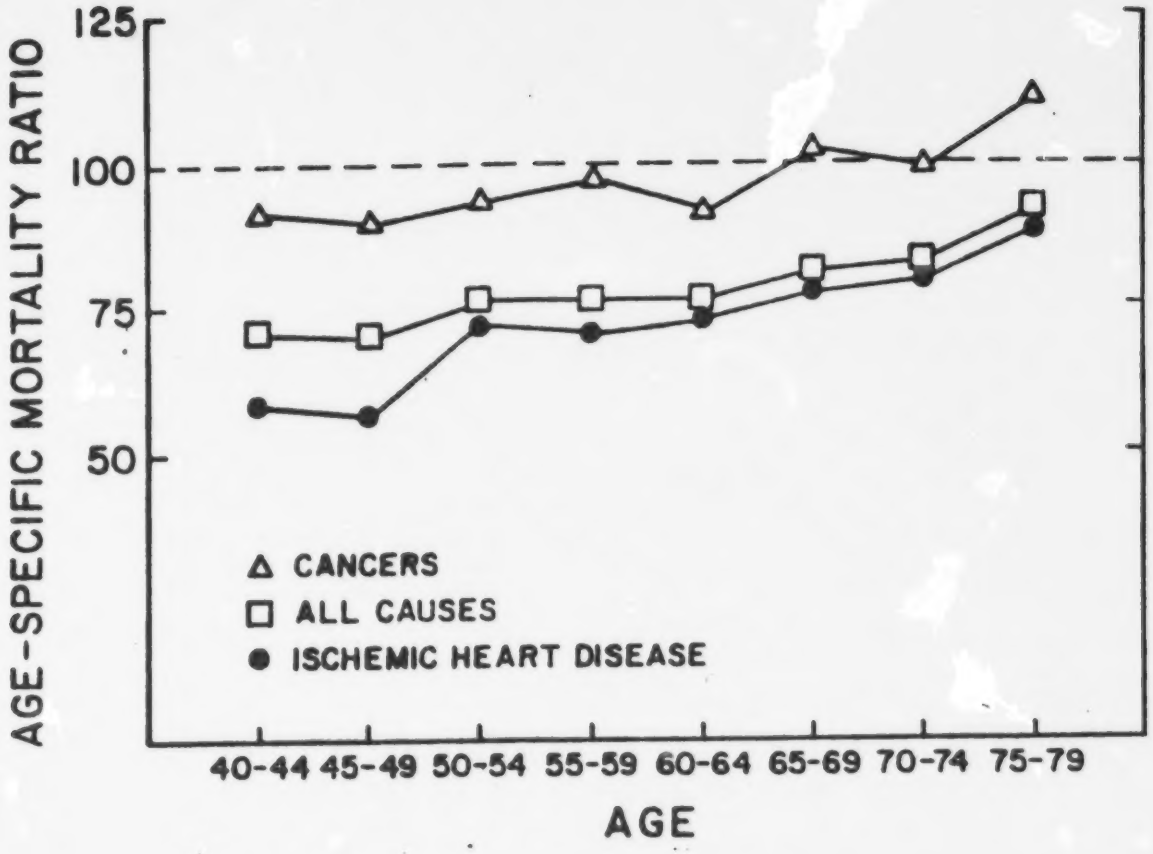


Figure 1
Schematic representation of the interrelated effects of occupational environment and lifestyle upon risk of cancer.



1. Expected deaths calculated from 1968 U. S. male age-specific death rates within 5-year age-bands.
2. Normal retirement occurs at age 65.

Fig 2. — Decline in healthy worker effect with age, male rubber workers.



Source: Graph based on tabular data from Milham, S. (1974).

Fig 3. — Considerable difference can occur in the healthy worker effect for different causes of death (carpenters and joiners).

THE HEALTHY WORKER EFFECT

by

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October 9, 1987

BACKGROUND

The panel requested from me, among others, a short paper on my experiences with the Healthy Worker Effect (HWE), the knowledge I derived from those, and the general beliefs/conclusions I now hold about the phenomenon -- with special reference to cancer research.

My insights into the HWE -- and other conceptual issues regarding epidemiologic research -- do not evolve inductively from experience with personal projects. Rather, their origin is my general devotion to theoretical epidemiology (1) -- my study of the subject, contemplation, and extensive involvement in consultation and teaching. (The teaching activities include an annual International Advanced Course on Epidemiologic Methods for researchers in occupational health epidemiology, given since 1971). Therefore, I respond directly to the Panel's third and final question, that is, the one about the conclusions I now believe to apply about the HWE -- in general and with special reference to occupational cancer epidemiology. I shall also elaborate in the rationale underlying my beliefs/conclusions and make a recommendation.

BELIEFS/CONCLUSIONS IN GENERAL

I believe/conclude that the concept of the HWE has arisen as the result of the following process of inference:

Premises:

1. Occupations have adverse effects on health.
2. Effects of occupations on health are manifest in contrasts between occupational cohorts and the "general" (national) population.

Observation:

Occupational cohorts tend to have more favorable health experiences than the "general" population.

Conclusion:

The premises, far from being brought to question by the observation, need to be refined in the light of it.

> Specifically, the second premise holds upon allowance for the HWE.

I believe/conclude this process of inference to be analogous to that which led to the concept of "negative flogiston": experience (burning of magnesium) led to observations (gain in weight) inconsonant with prevailing premises (the flogiston theory of burning, positing loss of flogiston and, hence, loss of weight); and the conclusion that was drawn that the premise (flogiston theory), far from being brought to question by the observation, needed to be refined in the light of the observations. Specifically, the prevailing concept that flogiston inherently had "positive" weight needed to be augmented by the concept of "negative flogiston", having "negative weight".

I also believe/conclude the concept of the HWE to be the result of erroneous reasoning, analogously with the genesis of the "negative flogiston" concept.

RATIONALE

I quote first from my textbook (1, pp. 30-32):

> Consider the study of the effect of some exposure, such as may occur in a particular occupation, on the occurrence of a particular illness. Presumably, the experience of an exposed population will be compared with that of a nonexposed one. However, non-exposure should not generally be taken simply as the absence of the exposure. Just as in clinical trials the treatment under study is contrasted with a "placebo" or "sham" treatment, exposure in a non-experimental study should be compared with what may reasonably pass as a corresponding "placebo" or "sham" category -- as an appropriate reference category of the determinant.
>
> The development of the definition of such a contrast, that is, of the index and reference categories on the empirical scale of the determinant, requires an express conceptualization of what aspect of the index category is under study -- as the counterpart of the drug or operation in a clinical regimen (involving various concomitant features whose effects are not under study). Thus, in an occupational study the aspect of interest may be stress in an air controller's occupation, asbestos exposure among misulators, vibration in the case of lumberjacks, or microwave exposure among radar operators. With the factor at issue in the index domain thus specified, on aims at seeing to it that the residual effect of the index category (e.g. occupation) on the health outcome under study is replicated in the reference category. This requirement of comparability of effects generally calls for the use of a subdomain of the non-exposure as the references category of the determinant. Those not meeting the criteria for either the index or the reference category fall in a third, "other", category of the determinant.

Example 2.6. In studying the effects of a particular occupation--of a particular aspect of it (see discussion above) -- the index category of the determinant represents employment in that occupation, naturally. The reference category should generally consist of particular other occupations, chosen expressly with a view to comparability of effects with the index occupation in terms of various extraneous effects of the compared occupation on the outcome(s) under study (cf. Wang and Miettinen, 1982)

The effect of the index category relative to the reference category is manifest in the empirical contrast only insofar as the compared populations, representing those categories, are comparable. This comparability of populations means that in the absence of differences in effect, the outcomes of the compared populations could be expected to be identical -- conditionally on whatever covariates will be controlled in the analysis. When individuals cannot be assigned randomly to the compared categories of the determinant, the empirical categories need to be defined with a view to comparability of populations.

In occupational mortality studies comparability of populations means that the compared occupations must have similar forces of job entry and job exit, insofar as these are related to indicators of risk for the mortality at issue, conditionally on controllable covariates (usually age and gender only).

Failure to appreciate this principle of contrast formation in the field of occupational health is at the root of the problem termed the healthy worker effect (MacMichael, 1976), that is, the tendency for observed mortality rates in particular occupational populations to be lower than would be "expected" on the basis of national rates (with allowance for differences in the distributions by age and gender, race, and calendar time).

The "healthy worker effect" -- or any healthy or sick "effect" -- is but a monument to habitual malpractice in the formation of contrasts (Miettinen, 1982 c; Wang and Miettinen, 1982), a consequence of epidemiology's intellectual traditions in demography (in addition to investigation of epidemics and the implementation of sample surveys) as against medical science (for which the paradigms might be pharmacologic laboratory studies and clinical trials). In the face of differential selection forces between/among the compared categories of the determinant, the need is to pursue a better empirical scale for the determinant, such that differential selection into and/or out of the compared categories would be minimized.

A somewhat different articulation of these issues is found in a recent address of mine to the International Society for Clinical Biostatistics (2):

The traditional epidemiologist, preoccupied with "general population", studies the effect of a potential etiologic agent by contrasting the exposed segment of that (or a related) "target population" with the remainder in it, that is, by contrasting exposure with non-exposure, unspecified [3,chs. 8-9].

In a clinical trail concerned with the effect of an agent (explanatory trial[4]), treatment with the agent is contrasted with comparable (identical) treatment without the agent (but with placebo), not with mere absence of the treatment involving the agent. This is understood to be necessary for isolating, empirically, the effect of the agent from that of the extraneous aspects of the treatment with the agent. (Only the theoretical contrast is, in its simplest terms, one between presence and absence of the agent[1, p. 30]).

The lesson to be gleaned from this, cardinal, feature of the clinical trial paradigm is that, in reference to any loosely defined source population in causality-oriented non-experimental research, the common two-point scale (exposure, non-exposure) for the determinant is generally indefensible. In the source population there are, at any given moment, people representing the (broad) empirical index category of the determinant, embodying the agent at issue (cf. treatment with agent); and there are, of course, people not representing the index category -- commonly the vast majority. Of the latter, non-index, segment of the source population, some represent a comparable reference category of the empirical scale of the determinant (cf. treatment with placebo); the remainder-- commonly the vast majority -- fall in the extraneous, "other" category of the determinant's empirical scale (cf. falling outside the realm of the clinical trial).

With this trichotomy pertaining to the source population, the study population is a subpopulation of it, consisting of representatives of the index and reference categories but not of the extraneous category, the clinical-trial paradigm being very clear on this. Thus, in non-experimental research the study population generally comprises only a small subsegment of the source population (to say nothing about "the general population" -- whatever the definition of the latter may be)[1, pp. 29-26, 218-227]. (A monument to the still common failure to appreciate the distinction between the non-index range of the empirical scale of the determinant and a proper reference category; as a subsegment of this range, is the concept and problem of "the healthy worker effect" -- arising from a contrast between an index cohort and "the general population" as the reference population[1, pp. 32-33].)

That the need to appreciate the essence of the experimental contrast as a paradigm in non-experimental epidemiologic research is not felt is, perhaps, the prime example of the "double standards[6] still prevalent between the experimental and non-experimental

modalities of cause-effect research -- with major implications for the validity of the latter.

BELIEF/CONCLUSION IN REFERENCE TO CANCER EPIDEMIOLOGY

It is my belief/conclusion that anyone who has proper appreciation of the seriousness of:

- the breach of scientific standards underlying the HWE, and - the imperative to assess occupational cancer risks with the highest attainable scientific standards,

would not knowingly, for whatever reasons of expediency, compromise both precepts.

That the practices underlying the HWE continue is, to me, a manifestation of the benightedness that still shrouds epidemiologic research modeled after its traditional paradigms (2).

RECOMMENDATION

I hold that the time has come to stop paying attention to research so primitive in design as to give rise to the HWE. To do otherwise would be a matter of continuing to allow healthy workers cloud due attention to workers' health.

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HEALTHY WORKER EFFECT

by
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September 1, 1987

HEALTHY WORKER EFFECT

My views on the healthy worker effect were recently published in a paper in the Journal of Occupational Medicine:

Monson R. R. Observations on the healthy worker effect. JOM 28:425-433, 1987.

The comments that follow will largely be a restatement of points made in that paper.

I believe that the healthy worker effect (HWE) is a straightforward example of confounding in epidemiologic data. The confounding factor is health status at entrance to follow-up, which may or may not be the same as entrance to employment. New and continuing workers logically have better health than members of the general population, which is made up of well and sick persons. Further, in order to continue work, persons must remain relatively healthy. Inasmuch as mortality rates for the general population are commonly used for comparison with the mortality rates of some employed healthy population, there is an over-estimation of deaths in the study population because of their better health status.

The healthy worker effect is related to cause of death in that diseases of old age are less related to health status at start of employment (or of follow-up) than are diseases of young age. Since most cancers are diseases of old age, the HWE tends to be less for cancer than for other causes of death. In my experience the HWE is strongest for non-malignant diseases of the respiratory, digestive, endocrine and urinary systems. Many of these diseases develop prior to age 20, so that they logically affect a person's ability to become employed in heavy industry. The HWE is moderate for diseases of the circulatory system, which account for 40-50% of all deaths. I am not aware of any consistent relation between the HWE and deaths from external causes. In particular, automobile accidents tend to be fatal in rural areas and non-fatal in urban areas.

While the healthy worker effect is usually presented in terms of relative risk (or standardized mortality ratio), one can also think of the HWE in absolute terms. The patterns of the relative and the absolute HWE in relation to length of survival differ considerably. The absolute HWE tends to remain fairly constant whereas the relative HWE tends to diminish. This "wearing-off" of the relative HWE does not necessarily reflect the development of work-related excess mortality. Rather, it probably is simply a reflection of the aging of the study population. If two populations differ at all ages by some constant absolute difference, and if the absolute rates in each population increase with age (and therefore with time), the absolute difference will become with time a relatively smaller percentage of the absolute rate. Therefore, the relative HWE will diminish.

In my paper I note that the HWE has two components - a dynamic phase and a plateau phase. During the dynamic phase of follow-up, say the first 10-20 years, the relative HWE diminishes. This occurs because of the aging of the population and because the study population is not constantly being replenished by newly hired, healthy workers. The plateau phase is a reflection of demographic differences between the study population and the general population and may or may not be present.

Examples of the presence of the healthy worker effect from my own studies are provided in the accompanying paper. In regard to cancer, I feel that in general the HWE can be ignored in analyses that use mortality rates (SMRs). However, this is not the case in analyses that use proportions (PMRs or MORs). Because cause-specific proportions are not independent, there is a tendency for the PMRs for cancer to be greater than 100; this is a reflection of the HWE for circulatory and other non-malignant diseases. Thus, a PMR of 115 for all cancer should be interpreted as no excess occurrence of cancer.

In reference to Dr. Howe's paper, I have the following comments:

a) I agree that a single parameter may not be sufficient to control the HWE. In paragraph 7d, page 432, of my paper I note that several factors must be taken into account in analyzing data that are affected by the HWE.

b) I agree that the HWE is unlikely to have any substantial influence upon the assessment of the causality of an association. I state this in paragraph 8 on page 432.

c) I agree that the use of an external population may increase the power relative to using an internal control group.

OBSERVATIONS ON THE HEALTHY WORKER EFFECT

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Follow-up mortality data from ten groups of employed persons are compared to the mortality rates of the United States general population. Comparisons related to the healthy worker effect (HWE) are computed. As measured by a relative comparison, the standardized mortality ratio (SMR), the HWE is seen to have a dynamic phase and a plateau phase in relation to length of follow-up. In contrast, the HWE as measured by an absolute comparison has little relationship to length of follow-up. Age at entrance into follow-up is strongly related to the absolute risk of mortality, but has little or no relation to the relative risk (SMR). Issues related to the evaluation and minimization of the healthy worker effect are discussed.

A continuing issue in the analysis of data from non-experimental follow-up studies is the basis of comparison. If the persons under observation can be separated into groups according to different levels of exposure, internal comparisons of rates are possible. However, if a group under observation is relatively uniform with respect to exposure, if the data are unstable, or if there are unresolvable concerns about possible confounding, comparison of the disease rates of the observation group with those of some external population may be desirable. Also, even if internal comparisons are possible, it may be of use to compare the study subgroups with an external population in order to assess which subgroup is more similar to the external population.

Historically, many studies of the long-term adverse effects of the workplace on health have compared the death rates of a group of employed persons to the death rates of the general population. In interpreting analyses of data where a study group is compared to the general population, there are issues of comparability. The population of the region from which the study group derives may have mortality rates that are different from those of the general population of the entire country. Further, if the study group has characteristics of health status that differ from those of the general population, during at least the early years of follow-up, differences in mortality rates would be expected. Persons who are ill will have higher rates and persons who are in good health will have lower rates than those of the general population.

Inasmuch as relatively good health is necessary for both initial and continuing employment, it has long been observed that groups of employed persons have mortality rates that are lower than rates for the general

population. This favorable mortality experience has been termed the healthy worker effect (HWE).[1] Uncertainty about the strength and extent of the HWE has led to uncertainty in interpreting data from studies in which the mortality rate of an employed group is compared with the mortality rate of the general population.

In this paper I describe the mortality experience in ten groups of employed persons in comparison to the mortality rates of the United States general population.

METHODS

Six independent groups of employed persons were evaluated: B. F. Goodrich rubber workers from Akron,[2,3,4,5,6] Boston fire fighters,[7] beryllium workers from Pennsylvania,[8] refinery workers,[9] smelter workers,[10] and US veterans.[11] Within the group of rubber workers, there were five independent subgroups: union white males, union black males, salaried males, union females, and salaried females. Except for the US veterans, the mortality experience of these persons was compared with that of the US general population using the USDR computer program.[12]

The basic method of comparison was to compute the person-years of follow-up for each study group, to multiply these person-years by the race-sex-age-time-cause specific mortality rates of the US general population in order to obtain the numbers of deaths expected in the study population, and to divide these expected deaths into the numbers observed. Most observations are presented as the observed/expected ratio. This relative ratio (RR) or standardized mortality ratio (SMR) is an approximation of the rate ratio or relative risk. Also, the attributable risk (AR) was approximated by computing the observed minus expected number of deaths per 1,000 person-years of follow-up. In order to evaluate the HWE further, data are also presented according to age at start of employment, year at start of employment, years since start of employment (latency), age at start of follow-up, and years since start of follow-up (survival). The abbreviation HWE(RR) is used to indicate the healthy worker effect as measured by the relative risk (SMR) and the abbreviation HWE(AR) indicates the healthy worker effect as measured by the attributable risk.

In general, follow-up did not start at initial employment but rather started at some specific date (e.g. Jan. 1, 1940) as well as after some minimum length of employment (e.g. 2 years). Except for the US veterans, each person was actively employed at start of follow-up. The veterans entered follow-up on the date of separation from active duty. Many persons were employed initially in the early 1900's or before.

Additional analyses were done for two groups: The B. F. Goodrich union white male rubber workers and the smelter workers. The group of rubber workers had no major excess mortality and thus provides data on the HWE. The group of smelter workers had excess mortality primarily from lung cancer, presumably because of exposure to arsenic. Therefore, these data are an example of work-related excess mortality.

As seen in Table 1, ten groups of workers were studied. The largest group on the basis of expected deaths is the union white male rubber workers. The group with the earliest start of follow-up (and thus the longest potential years of follow-up) is the Boston fire fighters. Persons were entered into follow-up at the beginning of the year of initial follow-up or at the date they started work plus the minimum years worked, whichever was later, and were continued in follow-up until death, the date of becoming lost to follow-up, or the common closing date.

RESULTS

In Table 2 RRs are presented for selected causes of death for each employed group. The RR for all causes is 1.0 for the Boston fire fighters (F) and is greater than 1.0 for the beryllium workers (H) and for the smelter workers (I). For the other groups the RR for all causes is less than 1.0, as is typical for most groups of employed persons. With the exception of the beryllium workers, the RR for all cancers is equal to or greater than the RR for all causes. The RRs for all circulatory diseases and for all causes other than cancer and circulatory diseases show no consistent differences from the RR for all causes. With the exception of the smelter workers, there is a tendency for the RR for external causes of death to be less than the RR for all causes.

In Table 3 the RRs for all causes are stratified on years since entrance into follow-up. In general, the RRs during the first 10 years of follow-up are less than the RRs during the succeeding years. This observation is the primary basis for the term "healthy worker effect." For the salaried female rubber workers (E) and for the beryllium workers (H) the RRs for the second 5 years of follow-up are less than those for the first 5 years. For each of the groups, the RR tends to increase with years of follow-up and to reach a plateau after some length of follow-up. This plateau is reached at 10 years for groups E through J, at 15 years for groups A and D, at 20 years for group C, and at 25 years for group B. The RR at the plateau is greater than 1.0 for groups H and I, reflecting probable work-related excess mortality. For the other groups the plateau ranges from 0.8 to 1.0, which may reflect basic demographic differences between a group and the general population. Thus, two characteristics of the pattern of the RR according to years of follow-up are observed: an initial dynamic increase and a stable plateau which may or may not be 1.0.

In Tables 4 to 13 data are presented for the B. F. Goodrich union white males. Data in Table 4 are RRs according to years of follow-up for selected causes of death. In general, the pattern for each category of cause of death reflects that of the all-causes category: there is an initial dynamic increase and a stable plateau after 10 to 20 years of follow-up. The RRs for all cancers and for all external causes are atypical in that the RRs during the first 5 years of follow-up are greater than those during the second 5 years. During the initial phase

of follow-up, the RR is least for nonmalignant respiratory and digestive diseases and is greatest for all cancers. During the plateau phase of follow-up, the RR is least for nonmalignant respiratory diseases and for all external causes and is greatest for all cancers.

Attributable or absolute risks (ARs) are presented in Table 5 according to the RR format of Table 4. The ARs are additive, as can be seen by the all-inclusive sum of the ARs for all cancers, all circulatory disease, and all other causes. For all causes, as well as for each cause of death, there is no apparent pattern in the ARs according to years of follow-up. Thus, there is little evidence for an HWE in any absolute sense. At least in this study group the HWE is only a relative observation.

In Tables 6 and 7 RRs and ARs are presented according to the year the employee started working and the years since he entered follow-up. Inasmuch as follow-up started on Jan. 1, 1940 or 2 years after the start of work, whichever was later, complete follow-up data are available only for the group that started work after Jan. 1, 1938. For persons in the other groups follow-up started after more than 2 years of work; persons who started work prior to 1920 had been actively employed for at least 20 years prior to entrance into follow-up. The age differences at entrance into follow-up between the four strata of workers can be seen in the average age at start of follow-up. However, in spite of these age differences, the strata show little difference in either the magnitude of the RRs or in the pattern according to years of follow-up. Each has an initial dynamic phase of follow-up where the RR increases from approximately 0.6 to approximately 0.8 and a stable plateau phase of approximately 0.9 that is reached after 15 years. During the dynamic phase the oldest group and the youngest group differ little. During the plateau phase the RR for the oldest group is about 10% greater than the RRs for the other groups.

By contrast, as seen in Table 7, there are major differences between the groups in the ARs. During the first 10 years of follow-up, the HWE in absolute terms is much greater among the older subgroups than among the younger ones. This is reflected in the marginal ARs. During the plateau phase two patterns can be examined. After 10 years of follow-up within each subgroup the ARs appear to stabilize. Also, within each 5-year period of follow-up, there is no consistent trend when going from the oldest group of workers to the youngest.

In Tables 8 and 9, RRs and ARs are presented according to the age at which the worker entered into follow-up and years since entering follow-up. As seen in Table 8, the two phases in the pattern of the RR are present for each age. The magnitude of the dynamic phase is similar for each age group. However, within the plateau phase, the RRs tend to be slightly greater as the age at entrance into follow-up increases. It can be inferred that the RR during follow-up after 65 years of age is 1.0. All persons in this study group had mandatory retirement at 65 years of age.

As with the pattern in AR according to the year the employee started work, the AR during the dynamic phase is strongly associated with age at entrance into follow-up (Table 9). Also, it can be seen that during the active work years of the study group, the Ar is associated with age during the plateau phase in a manner similar to the association during the dynamic phase. Only after persons still in follow-up reach 65 years of age does the AR become closer to zero.

In Tables 10 and 11, the RRs and Ars are cross-classified according to age at entrance into follow-up and year started working. In Table 10, the year the employee started working shows little association with the RR, whereas there is a slight trend in the RR according to age at entrance into follow-up. In Table 11, the marginal age trend is stronger than the marginal year trend. Within the body of the table, the data are inconsistent. With the exception of those who enter follow-up at 55 years of age and older, there is a decreasing trend in the AR with an increase in the year the person started working. The increase in the AR according to age at entrance into follow-up is generally present except for persons who started work before 1920.

RRs and ARs are stratified in Tables 12 and 13 according to age at start of work and years since work started instead of age and years in relation to follow-up. By examining data in this manner it is possible to evaluate possible causal associations in relation to work. Follow-up per_se is of course a characteristic of the study design rather than of the group under observation. In some studies follow-up starts at or near the start of work, so that survival and latency are synonymous.

In Table 12, as in Table 8, there is both a dynamic phase and a plateau phase in the RR. The dynamic phase lasts for 30 years rather than for 15 years, probably because latency is not highly correlated with survival. However, as in Table 8, age at start of work shows little relation with the RR. The data in Table 9 and in Table 13 are more comparable to each other, in that there is a decrease in the AR with an increase in age. There is little trend in the AR with increasing latency until 35 years after work started. The decrease after this time is due primarily to low ARs in the youngest groups at ages just before normal retirement.

In the remaining tables, data from the smelter workers are presented. In Tables 14 and 15 RRs and ARs are presented according to age at entrance into follow-up and years since entering follow-up. As seen in Table 14, the dynamic phase for the HWE lasts for no more than 5 years and is weak or nonexistent. The excess RRs during the plateau phase are stable and show no association with age at entrance into follow-up. However, as seen in Table 15, the (excess) AR is strongly associated with age. During the dynamic phase the AR tends to become more negative with age at entrance into follow-up, although the pattern is not stable. During the plateau phase, there is a strong positive association between the AR and age at entrance into follow-up. Further, there is an unstable tendency for the AR to increase with increasing follow-up

within each category. Each age-at-entrance subgroup is of course aging about 5 years during each five-year period of follow-up.

Because the greatest excess RR among smelter workers is seen for lung cancer, data are presented in Tables 16 to 18 for this cause of death. The causal excess of lung cancer overwhelms any tendency in an HWE, thus these data should be viewed in a different light. As seen in Table 16, the RR increases in a stable manner with increasing age at entrance into follow-up, but shows little association according to years since entering follow-up. In Table 17, the AR not only increases with increasing age at entrance, but also increases as follow-up becomes longer. As with the HWE, it can be seen that the RR and the AR have different patterns when a causal excess is present.

However, whereas the HWE is an observation that is related to follow-up, a causal RR is more related to characteristics of work. Thus, in Tables 18 and 19, RRs and ARs for lung cancer among smelter workers are presented according to age at start of work and years since work started (latency). In Table 18 the RR shows no consistent relation to age at start of work. At under 15 years of latency a slight excess is seen. Thereafter, the trend in RR is inconsistent until 40 years after start of work before 25 years of age have had more follow-up at 40 or more years of latency than have workers in the other age groups, the marginal RR for this group is higher. In general, however, the excess RR for lung cancer is relatively stable after 15 years of follow-up, that is, the adverse effects (presumably of arsenic) continue for at least 45 years.

As seen in Table 19, the AR for excess lung cancer tends to increase with increasing follow-up. The trend according to age at start of work is less consistent, but the AR tends to be greater as age increases.

DISCUSSION

At least since the observations of Ogle,[13] it has been recognized that methodologic concerns affect the interpretation of data on the mortality of occupational groups. Initiated by a letter to the editor of the Journal of Occupational Medicine,[14] an extensive discussion has been carried out in the literature of occupational epidemiology during the past 10 years. A number of points about the HWE have been raised, and differing opinions have been offered by different observers. I will phrase these points as questions and will offer my opinion based in part on the data in this paper.

List of Points in the Literature Related to the Healthy Worker Effect

1. Is the healthy worker effect due to selection bias or to confounding?[6,11,15,16,17]

In my view, selection bias occurs because of the actions of the investigator, whereas confounding is a characteristic of the study population. It follows from this that the HWE is an example of

confounding. The confounding factor is the (unmeasured) health status of the group of employees. If it were possible to measure this variable in both the study population and in the general population, one could control for the HWE as for any confounding factor.

In contrast, a selection bias would result if the investigator used information on outcome (fact or cause of death) in defining the study population. Such a bias is unlikely when the study population is defined from work records, although it is possible if the records of deceased persons are kept separate from the records of living persons. Selection bias is a major concern in studies where the data are based solely on death certificates. Under this circumstance, it is unlikely that all deaths in the undefined study population have been ascertained, and it is possible that deaths due to a cause of interest, say, cancer, may have been selectively ascertained.

The disagreement about the nature of the HWE is largely a matter of semantics. Clearly, there is selection of healthier persons into the work force, and this selection leads to a difference between a population of workers and the general population. However, in a formal sense it seems better to view the HWE as an example of confounding rather than selection bias.

2. Is the healthy worker effect related to cause of death?[6,11,15,18,19] Specifically, is the HWE for all cancers less than that for all causes?

It is frequently observed in follow-up studies of employed persons where there is an overall HWE that the standardized mortality ratio for all cancers lies between that for all causes and 100. This observation has led to a view that the HWE is of little or no consequence in interpreting data on cancer mortality. Further, this observation is intuitively appealing, in that factors that predict eventual death from cancer are less likely to be present at 20 years of age, when many persons become employed, than are factors that may predict deaths from other causes.

The data in Table 2 and in Table 4 are consistent with this view. For five of the seven groups with RRs for all causes at less than 1.0, the RR for all cancers is closer to 1.0. For the other two groups (C and D), the RRs for all causes, all cancers, and all circulatory disease differ little. Also, as seen in Table 4, among the B. F. Goodrich white male union employees after 15 years of follow-up, the RR for all cancers is 1.0 whereas that for all causes is 0.9.

In contrast the RRs for all circulatory diseases differ little from the RRs for all causes (Table 2). Of course, circulatory diseases account for about half of all deaths. During the first 15 years of follow-up, the lowest RRs are seen for nonmalignant respiratory and digestive diseases (Table 4). Although these are not common causes of death, potentially fatal diseases such as asthma and colitis are manifest by age 20 and are a factor in employment.

RRs for all external causes are likely to be the most variable from group to group. The major category of cause of death under this rubric is automobile accidents. Populations that are largely rural will have higher death rates from accidents than populations that are largely urban.

3. Is the healthy worker effect related to age?[14,19,20]

Fox and Collier observed that the SMR for all causes was lower at young ages than at old ages.[15] Age in their paper refers to age attained or chronologic age. It is clear from the data in their Table 1 that this association between the SMR and age attained was due to confounding by latency. The SMRs at older ages reflected the greater SMRs present at longer years of latency. Thus, it is questionable whether attained age per se is a useful factor to use in examining the HWE.

Based on the data in Tables 8 and 12 of this paper, age at entrance into follow-up as well as age at start of work show little relation to the HWE(RR). Any crude associations seen are due more to years of survival or of latency than to age per se. However, in evaluating the HWE(AR), age at start of work, age at entrance into follow-up, and probably age attained are strongly associated with the AR.

Thus, it follows that in routine presentation of data from follow-up studies, stratification on any measure of age is unlikely to be of major use.

4. How do relative risk comparisons relate to absolute risk comparisons?[16,21]

Based on the data in this paper, there are clear differences between relative and absolute measures of risk. For most causes of death the HWE(RR) diminishes with length of follow-up, but the HWE(AR) changes inconsistently or not at all. Relative measures are more common in the epidemiologic literature, presumably because they are intuitively simple and easy to compare to each other. However, in the assessment of magnitude of risk, for example, cancer caused by exposure to radiation, absolute measures have become commonplace. Further presentation of absolute measures of risk in occupational groups would be of value to assess its utility.

5. How long does the healthy worker effect last?[15]

Fox and Collier observed that in their cohort of vinyl chloride workers the HWE lasted about 15 years.[15] (In their study, follow-up started at start of work, so that latency and survival were synonymous.) For the B. F. Goodrich rubber workers, also, the dynamic phase of the HWE(RR) lasted about 15 years (Table 2). However, for other groups, the dynamic phase of the HWE(RR) was observed for as few as 5 years or for as long as 25 years. Further, as seen in Table 4, the dynamic phase was of different duration for different causes of death.

6. What factors contribute to the healthy worker effect?[15,16,19,22,23,24]

Fox and Collier[15] conclude that the HWE has three components:

a) Selection of a healthy population for employment;
b) Survival in industry of the healthier men;
c) Length of time that the population has been pursued (followed).

Wen and Tsai[16] and Wen et al.[22] list three factors that affect the HWE as expressed by SMRs:

a) Selection bias;
b) Improved socioeconomic status;
c) The conventional way of calculating SMRs. In this they include the characteristics of indirect standardization, considerations of life expectancy, and a diminishing number of active workers.

McMichael[19] notes that the HWE differs according to age group, race, work status, cause of death, and elapsed-time period of observation.

Koskela et al.[23] emphasize the importance of distinguishing a cross-sectional cohort from an open cohort. A cross-sectional cohort is composed of persons active at one point in time, whereas an open cohort is composed of all new persons hired during some period of time.

The above factors can be classified into two general categories that contribute to the healthy worker effect:

a) Selection of healthier workers both at initial employment and during continuing employment;
b) Demographic differences between the study population and the external (general) population whose rates are used for comparison.

These two categories correspond generally to the two phases observed in the HWE data. There is almost always a dynamic phase of the HWE that lasts for the first 10 to 20 years of follow-up. The HWE(RR) diminishes during this phase because the initial relative health advantage that employed persons have is diluted by the subsequent development of ill health. There may or may not be a plateau phase of the HWE(RR), depending whether or not the external comparison rates accurately reflect the basic mortality of the study population.

It should be noted that the dynamic phase of the HWE(RR) is present both in cross-sectional and in open cohorts, as long as all persons are actively employed at start of follow-up. Further, age at entrance into follow-up does not seem to be strongly related to the HWE(RR), as noted from the B. F. Goodrich data. However, in a cross-sectional or closed cohort, the dynamic phase of the HWE(RR) would be expected to wear off sooner than in an open cohort, in that the population is not being replenished by new, healthy employees.

It should also be noted that the dynamic phase of the HWE(RR) is related more strongly to years of survival than to years of latency. In a sense it is an artificial characteristic of the study design. However, the plateau phase is or is not present at all years of survival or of latency and is a characteristic of the study population.

7. Will the development of a standard comparison of employed persons diminish or eliminate the healthy worker effect?[14,20,23,24]

A number of authors have suggested assembling a large group of employed persons and using their mortality rates as the standard basis for external comparison in studies of groups of employed persons. It has been argued that this would largely eliminate the problem of the healthy worker effect.

However, several points must be made if mortality rates from such a group are to be used in place of rates from the general population:

a) The group must be large so that the rates are stable;

b) The plateau phase of the HWE will not necessarily be eliminated if there are demographic differences between the study population and the industrial comparison population. Although it seems reasonable that an industrial comparison population would be more comparable to a group of employed persons than the general population with respect to socioeconomic status, there may be other important demographic differences such as ethnicity or region.

c) The dynamic phase of the HWE may not be altered at all, unless length of survival is taken into account in both the study population and the comparison population. Simply having age-time-sex-race-cause specific rates to use for comparison will not automatically eliminate the dynamic phase of the HWE(RR).

d) Because of the need for simultaneous control of at least age and year at start of work, age and year at start of follow-up, length of work, and length of survival, multivariate analysis will be necessary.[25] Traditional SMR analyses will continue to be useful to describe the mortality in populations and to screen data for associations that can better be quantified by multivariate techniques.

8. Finally, in interpretation of data where there is apparent work-related excess mortality, the healthy worker effect may often be ignored. As seen in Tables 16 to 19, lung cancer is in excess among smelter workers during all years since entering follow-up as well during all years of latency. The healthy worker effect is relatively weak in comparison to causal excesses that can be detected in epidemiologic data.

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TABLE 1

CHARACTERISTICS OF OCCUPATIONAL COHORTS ANALYZED

	Total No.			Year of Initial Follow-Up	Average Age at Entrance to Follow-up	Common Closing Date	Minimum Years Worked
	Persons	Person Years	Expected Deaths				
Rubber workers							
- union white males	15,643	442,000	7812	1940	36	1978.5	2
- union black males	1,184	28,700	473	1940	32	1978.5	2
- salaried males	4,683	110,600	1530	1940	33	1978.5	2
- union females	4,610	145,000	1257	1940	34	1978.5	2
- salaried females	3,401	81,600	342	1940	27	1978.5	2
Boston fire fighters	4,715	109,500	1771	1925	34	1975.0	3
Refinery workers	10,840	214,200	3564	1937	29	1978.0	0
Beryllium workers	3,051	72,300	811	1942	32	1977.0	0
Smelter workers	8,042	190,900	2729	1938	35	1977.8	1
US veterans	85,491	?	6402	1947	?	1970.0	?

TABLE 2

OBSERVED/EXPECTED RATIO OF DEATHS AMONG VARIOUS GROUPS OF EMPLOYED PERSONS ACCORDING TO SELECTED CAUSES OF DEATH·

Group	Cause of Death				
	All Causes	All Cancers	Circulatory Diseases	ACOCC+	External
A	0.9	1.0	0.9	0.9	0.6
B	0.7	0.8	0.8	0.6	0.5
C	0.7	0.7	0.7	0.7	0.4
D	0.8	0.8	0.8	0.9	0.8
E	0.7	0.8	0.6	0.8	0.7
F	1.0	1.0	1.0	0.9	0.8
G	0.9	1.0	0.8	0.9	0.8
H	1.1	1.0	1.2	1.0	1.0
I	1.2	1.3	1.1	1.3	1.5
J	0.8	0.9	0.8	0.9	0.9

· See Table 1 for description of groups.
+ All causes other than cancer and circulatory diseases.

TABLE 3

OBSERVED/EXPECTED DEATHS AMONG VARIOUS GROUPS OF EMPLOYED PERSONS ACCORDING TO YEARS SINCE ENTERING FOLLOW-UP·

Group	Years Since Entering Follow-up						Total
	0-4	5-9	10-14	15-19	20-24	≥25	
A	0.6	0.7	0.8	0.9	0.9	0.9	0.9
B	0.3	0.5	0.5	0.7	0.8	0.9	0.7
C	0.4	0.6	0.5	0.7	0.8	0.8	0.7
D	0.5	0.8	0.8	0.9	0.7	0.9	0.8
E	0.8	0.6	0.8	0.7	0.8	0.7	0.7
F	0.8	0.8	1.0	0.9	1.0	1.0	1.0
G	0.8	0.8	0.9	0.9	0.9	0.9	0.9
H	0.9	0.8	1.3	1.0	1.1	1.2	1.1
I	0.9	1.2	1.4	1.4	1.3	1.2	1.2
J	0.8	0.8	0.9	0.9	0.9	---	0.8

· See Table 1 for description of groups.

TABLE 4

OBSERVED/EXPECTED DEATHS AMONG UNION WHITE MALE RUBBER WORKERS ACCORDING TO CAUSE OF DEATH AND YEARS SINCE ENTERING FOLLOW-UP

Cause of Death	Years Since Entering Follow-up						
	0-4	5-9	10-14	15-19	20-24	≥25	Total
All causes	0.6	0.7	0.8	0.9	0.9	0.9	0.9
All cancers	0.9	0.8	0.8	1.0	1.0	1.0	1.0
All circulatory	0.7	0.8	0.8	0.9	0.8	0.9	0.9
All causes other than cancer and circulatory	0.5	0.7	0.8	1.0	0.9	1.0	0.9
Lung cancer	0.7	0.8	0.7	1.0	1.0	0.9	0.9
Nonmalignant respiratory disease	0.4	0.4	0.6	0.7	0.6	0.9	0.7
Nonmalignant digestive diseases	0.4	0.7	0.8	0.8	1.1	0.9	0.8
All external causes	0.6	0.5	0.7	0.6	0.7	0.7	0.6

TABLE 5

OBSERVED-EXPECTED DEATHS/1,000 PERSON-YEARS OF FOLLOW-UP AMONG UNION WHITE MALE RUBBER WORKERS ACCORDING TO CAUSE OF DEATH AND YEARS SINCE ENTERING FOLLOW-UP

Cause of Death	Years Since Entering Follow-up						
	0-4	5-9	10-14	15-19	20-24	≥25	Total
All causes	-2.3	-2.5	-2.0	-1.3	-2.5	-2.5	-2.3
All cancers	-0.1	-0.3	-0.4	-0.1	0.1	-0.0	-0.1
All circulatory	-0.7	-0.9	-1.0	-0.9	-1.7	-2.3	-1.3
All causes other than cancer and circulatory	-2.0	-1.3	-0.7	-0.3	-0.9	-0.2	-0.9
Lung cancer	-0.0	-0.0	-0.1	-0.0	-0.0	-0.3	-0.1
Nonmalignant respiratory	-0.2	-0.2	-0.2	-0.2	-0.5	-0.4	-0.3
Nonmalignant digestive	-0.3	-0.1	-0.1	-0.2	-0.1	-0.1	-0.1
All external causes	-0.5	-0.5	-0.3	-0.5	-0.4	-0.5	-0.5

TABLE 6

OBSERVED/EXPECTED DEATHS AMONG UNION WHITE MALE RUBBER WORKERS ACCORDING TO YEAR STARTED WORKING AND YEARS SINCE ENTERING FOLLOW-UP·

Year Started Working	Years Since Entering Follow-up						Average Age at Start of Follow-up
	0-4	5-9	10-14	15-19	≥20	Total	
<1920	0.6	0.7	0.9	1.0	1.0	0.9	52
1920-29	0.5	0.6	0.8	0.9	0.9	0.9	43
1930-37	0.7	0.8	0.7	0.9	0.9	0.9	33
≥1938	0.6	0.8	0.8	0.9	0.9	0.9	31
Total	**0.6**	**0.7**	**0.8**	**0.9**	**0.9**	**0.9**	**36**

· Follow-up started on Jan. 1, 1940 or on the second anniversary of employment, whichever was later.

TABLE 7

OBSERVED-EXPECTED DEATHS/1,000 PERSON-YEARS OF FOLLOW-UP AMONG UNION WHITE MALE RUBBER WORKERS ACCORDING TO YEAR STARTED WORKING AND YEARS SINCE ENTERING FOLLOW-UP·

Year Started Working	Years Since Entering Follow-up					
	0-4	5-9	10-14	15-19	≥20	Total
<1920	-7.1	-6.3	-2.4	-1.0	-0.9	-3.5
1920-29	-4.5	-5.5	-3.3	-2.9	-3.9	-4.0
1930-37	-1.5	-1.2	-2.7	-1.4	-3.0	-2.2
≥1938	-1.8	-1.1	-1.3	-0.6	-1.3	-1.2
Total	**-2.8**	**-2.5**	**-2.0**	**-1.2**	**-2.3**	**-2.2**

· Follow-up started on Jan. 1, 1940 or on the second anniversary of employment, whichever was later.

TABLE 8

OBSERVED/EXPECTED DEATHS AMONG UNION WHITE MALE RUBBER WORKERS ACCORDING TO AGE AT ENTRANCE INTO FOLLOW-UP AND YEARS SINCE ENTERING FOLLOW-UP

Age at Entrance into Follow-up	Years Since Entering Follow-up					
	0-4	5-9	10-14	15-19	≥20	Total
<25	0.6	0.9	0.9	0.8	0.9	0.8
25-34	0.6	0.6	0.8	0.9	0.8	0.8
35-44	0.7	0.6	0.7	0.9	0.9	0.8
45-54	0.6	0.8	0.8	1.0	1.0	0.9
≥55	0.6	0.8	1.0	1.0	1.0	0.9
Total	**0.6**	**0.7**	**0.8**	**0.9**	**0.9**	**0.9**

TABLE 9

OBSERVED-EXPECTED DEATHS/1,000 PERSON-YEARS OF FOLLOW-UP AMONG UNION WHITE MALE RUBBER WORKERS ACCORDING TO AGE AT ENTRANCE INTO FOLLOW-UP AND YEARS SINCE ENTERING FOLLOW-UP

Age at Entrance into Follow-up	Years Since Entering Follow-up					
	0-4	5-9	10-14	15-19	≥20	Total
<25	-0.9	-0.2	-0.2	-0.7	-1.1	-0.7
25-34	-0.0	-1.1	-1.0	-0.9	-3.5	-1.7
35-44	-2.0	-2.8	-3.5	-2.7	-3.5	-2.9
45-54	-6.0	-5.8	-4.6	-1.0	-1.0	-3.5
≥55	-13.1	-9.2	-1.6	-0.4	-0.9	-5.6
Total	-2.8	-2.5	-2.0	-1.2	-2.3	-2.2

TABLE 10

OBSERVED/EXPECTED DEATHS AMONG UNION WHITE MALE RUBBER WORKERS ACCORDING TO AGE AT ENTRANCE INTO FOLLOW-UP AND YEAR STARTED WORKING

Age at Entrance Into Follow-up	Year Started Working				
	<1920	1920-29	1930-37	≥1938	Total
<25	---	---	0.8	0.9	0.8
25-34	---	0.7	0.8	0.9	0.8
35-44	0.8	0.9	0.9	0.9	0.9
45-54	0.9	0.9	1.0	0.9	0.9
≥55	0.9	0.9	0.7	0.9	0.9
Total	**0.9**	**0.9**	**0.9**	**0.9**	**0.9**

TABLE 11

OBSERVED-EXPECTED DEATHS/1,000 PERSON-YEARS OF FOLLOW-UP AMONG UNION WHITE MALE-RUBBER WORKERS ACCORDING TO AGE AT ENTRANCE INTO FOLLOW-UP AND YEAR STARTED WORKING

Age at Entrance Into Follow-up	Year Started Working				
	<1920	1920-29	1930-37	≥1938	Total
<25	---	0	-1.5	-0.6	-0.7
25-34	---	-3.9	-2.4	-0.7	-1.7
35-44	-4.3	-3.1	-2.8	-2.4	-2.9
45-54	-3.4	-5.1	0.9	-2.9	-3.5
≥55	-3.3	-6.3	-19.2	-6.9	-5.6
Total	**-3.5**	**-4.0**	**-2.2**	**-1.2**	**-2.2**

TABLE 12

OBSERVED/EXPECTED DEATHS AMONG UNION WHITE MALE RUBBER WORKERS ACCORDING TO AGE AT START OF WORK AND YEARS SINCE WORK STARTED

Age at Start of Work	Years Since Work Started (Latency) 0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	≥40	Total
<25	0.6	0.6	0.8	0.8	0.7	0.7	0.9	0.8	0.9	0.8
25-34	0.5	0.5	0.8	0.7	0.7	0.8	0.9	0.8	1.0	0.9
35-44	1.1	0.9	0.7	0.7	0.9	0.9	1.0	1.1	1.0	0.9
45-54	0.5	0.6	0.8	0.9	1.1	0.9	0.8	1.1		0.9
≥55	0.1·	1.0	1.0	1.0	1.0	0.8	1.1	---		0.9
Total	**0.6**	**0.7**	**0.8**	**0.8**	**0.8**	**0.8**	**0.9**	**0.9**	**0.9**	**0.9**

· Two observed, 14.3 expected

TABLE 13

OBSERVED-EXPECTED DEATHS/1,000 PERSON-YEARS OF FOLLOW-UP AMONG UNION WHITE MALE RUBBER WORKERS ACCORDING TO AGE AT START OF WORK AND YEARS SINCE WORK STARTED

Age at Entrance into Follow-up	Years Since Work Started (Latency) 0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	≥40	Total
<25	-0.8	-0.8	-0.5	-0.7	-1.6	-2.1	-1.8	-3.9	-5.2	-1.8
25-34	-1.3	-1.5	-1.1	-2.0	-3.3	-3.4	-2.0	-5.7	-2.4	-2.5
35-44	-0.3	-0.6	-3.3	-5.5	-1.9	-3.8	-0.4	5.6	1.3	-2.0
45-55	-7.2	-7.8	-5.6	-4.9	-3.7	-7.0	-21.0	18.2		-5.4
≥55	-23.9	-1.7	-1.7	-3.1	-1.8	-35.2	4.7	---		-7.1
Total	**-1.7**	**-1.4**	**-1.4**	**-2.1**	**-2.1**	**-3.1**	**-2.1**	**-3.7**	**-3.5**	**-2.2**

TABLE 14

OBSERVED/EXPECTED DEATHS AMONG SMELTER WORKERS ACCORDING TO AGE AT ENTRANCE INTO FOLLOW-UP AND YEARS SINCE ENTERING FOLLOW-UP

Age at Entrance into Follow-up	Years Since Entering Follow-up					
	0-4	5-9	10-14	15-19	≥20	Total
<25	0.9	1.0	2.0	1.6	1.4	1.4
25-34	1.0	1.5	1.4	1.3	1.2	1.2
35-44	1.0	1.2	1.5	1.6	1.2	1.3
45-54	1.0	1.4	1.2	1.3	1.2	1.2
≥55	0.8	1.1	1.4	1.4	1.1	1.1
Total	**0.9**	**1.2**	**1.4**	**1.4**	**1.2**	**1.2**

TABLE 15

OBSERVED-EXPECTED DEATHS/1,000 PERSON-YEARS OF FOLLOW-UP AMONG SMELTER WORKERS ACCORDING TO AGE AT ENTRANCE INTO FOLLOW-UP AND YEARS SINCE ENTERING FOLLOW-UP

Age at Entrance into Follow-up	Years Since Entering Follow-up					
	0-4	5-9	10-14	15-19	≥20	Total
<25	-0.2	0.0	2.0	1.6	3.3	1.6
25-34	-0.1	1.7	1.7	1.8	3.7	2.1
35-44	0.0	1.2	5.5	10.7	7.7	5.0
45-54	-0.6	8.3	5.6	10.6	13.7	7.0
≥55	9.7	7.0	26.7	30.0	9.8	8.8
Total	**-1.0**	**2.3**	**4.4**	**5.4**	**5.3**	**3.4**

TABLE 16

OBSERVED/EXPECTED DEATHS FROM LUNG CANCER AMONG SMELTER WORKERS ACCORDING TO AGE AT ENTRANCE INTO FOLLOW-UP AND YEARS SINCE ENTERING FOLLOW-UP

Age at Entrance into Follow-up	Years Since Entering Follow-up					
	0-4	5-9	10-14	15-19	≥20	Total
<25	---·	---	---	---	1.2	1.1
25-34	---	---	---	3.4	1.8	1.9
35-44	---	2.6	1.8	3.1	2.2	2.3
45-54	2.5	3.7	1.7	2.9	2.0	2.4
≥55	5.3	3.0	1.8	3.7	4.7	3.6
Total	**3.3**	**3.0**	**1.6**	**3.0**	**1.9**	**2.2**

·--- = fewer than two deaths expected; nc excess lung cancers.

TABLE 17

OBSERVED-EXPECTED DEATHS FROM LUNG CANCER/1,000 PERSON-YEARS OF FOLLOW-UP AMONG SMELTER WORKERS ACCORDING TO AGE AT ENTRANCE INTO FOLLOW-UP AND YEARS SINCE ENTERING FOLLOW-UP

Age at Entrance into Follow-up	Years Since Entering Follow-up					
	0-4	5-9	10-14	15-19	≥20	Total
<25	---·	---	---	---	0.1	0.0
25-34	---	---	---	0.9	1.2	0.5
35-44	---	0.5	0.5	2.4	3.0	1.4
45-54	0.6	2.1	1.0	3.9	3.0	1.9
≥55	2.2	1.7	1.0	4.6	8.9	2.7
Total	**0.3**	**0.5**	**0.2**	**1.3**	**1.3**	**0.8**

· See Table 16 legend.

TABLE 18

OBSERVED/EXPECTED DEATHS FROM LUNG CANCER AMONG SMELTER WORKERS ACCORDING TO AGE AT START OF WORK AND YEARS SINCE WORK STARTED

Age at Start of Work	Years Since Work Started (Latency)							
	<15	15-19	20-24	25-29	30-34	35-39	≥40	Total
<25	---·	---	0.8	2.4	2.2	2.1	3.2	2.6
25-34	---	2.1	1.5	1.8	1.9	2.9	3.4	2.1
35-44	1.1	2.8	2.6	1.6		1.9		2.1
≥45	1.7	1.7		1.6	---	---	---	1.6
Total	**1.4+**	**2.1**	**1.6**	**2.0**	**1.7**	**2.0**	**3.3**	**2.2**

· See Table 16 legend.
+ 21 observed/15.2 expected.

TABLE 19

OBSERVED-EXPECTED DEATHS FROM LUNG CANCER/1,000 PERSON-YEARS OF FOLLOW-UP AMONG SMELTER WORKERS ACCORDING TO AGE AT START OF WORK AND YEARS SINCE WORK STARTED

Age at Start of Work	Years Since Work Started (Latency)							
	<15	15-19	20-24	25-29	30-34	35-39	≥40	Total
<25	---·	---	-0.0	0.8	0.8	1.2	6.1	0.7
25-34	---	0.4	0.4	0.8	1.3	1.0	5.5	0.7
35-44	0.0	2.0	2.8	1.4		2.7		1.1
≥45	0.7	1.5		1.7	---	---	---	1.0
Total	**0.1**	**0.5**	**0.4**	**0.9**	**0.9**	**1.4**	**4.9**	**0.8**

· See Table 16 legend.

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COMMENTS ON THE HEALTHY WORKER EFFECT

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INTRODUCTION

The "healthy worker effect", (HWE) is a term applied to deficits of mortality ascribed to various factors associated with employment. These can best be categorized as selection factors in hiring and in continued employment. Table 1 lists some of these factors. They are of most importance in cohort studies when the comparison mortality or morbidity estimates use general population rates, rather than those of a comparison working population. The requirement of good health at the time of hire can lead to observed deficits of mortality from all causes for as long as ten years in a work population compared to the general populations. Selection for cancer risk is much less long lasting, but deficits may exist for two or three years in carefully screened populations. To the extent that heavy smokers or consumers of alcohol are excluded at the time of hire, there may also be a selection based upon personal habits. This factor influences mortality for much longer periods of time. To the extent that selection for general health and personal habits exist in the hiring process, it is likely to lead to lower mortality and morbidity rates than would be present in the general population. However, while overall rates would be lowered, deceptively positive trends according to years since employment could be noted as the effect of hiring selection wanes.

OBSERVATIONS OF THE HWE

Table 2 lists some SMR's observed in populations studied at Mt. Sinai. In the case of groups exposed to PCBs and styrene deficits were observed in virtually all listed causes. In neither study was it possible to associate any excess mortality, e.g. from lymphoma or leukemia, to exposure. This, however, was not precluded by the existence of a HWE, but by the limited power of the study. In the case of vinyl chloride, deficits existed in all cause mortality despite an extraordinary risk of liver hemangiosarcoma.

In the study of printing pressmen, a problem opposite to that of a HWE was faced. Strong arguments were made by industry sources that the social habits of pressmen accounted for most of the excess cancer mortality, particularly that of lung cancer. This was investigated by establishing that there was not the expected increases in the various smoking related causes of death were all the lung cancer increase the result of cigarette smoking. Further, while cancer of the lung and oral

cancer (sites of excess cancer in the study) could be related to unusually higher alcohol and cigarette consumption, a statistically significant, more than two-fold, increase in death from skin cancer could not.

In the studies of the asbestos groups, the agent related mortality was so great the presence of any HWE played no role in the study evaluations.

Table 3 lists SMR's that are likely to represent the upper range of possible effects from hiring selection factors. The SMR's are those found in various studies of laboratory and industrial workers employed by national nuclear energy establishments. Here, because of stringent employment hiring practices, the HWE would be expected to be important. Further, the studies were large, so the observed SMR's have narrow confidence limits. As can be seen, deficits of mortality of approximately 20% exist for all listed causes. This probably represent the largest effect that might be observed in any given study.

Job selection may also be influenced by personal habits and physical condition. The well-known study of cardiovascular disease in relation to physical activity among London bus drivers and conductors well illustrates the point. Lower mortality was initially attributed to conductors because of their more active work (climbing stairs on the London double-decker buses) (11). However, a follow-up analysis indicated that those individuals chosen for bus driving or selecting that task were considerably heavier at the time of hire than their colleagues chosen as conductors (12). Without controlling for weight or health status at hire, any mortality differences ascribed to activity were invalid.

The availability of quality medical care by virtue of funded programs for work populations can affect the incidence and mortality from various diseases. Firstly, earlier intervention can prevent deaths that would otherwise occur were frequent medical care not utilized. In other circumstances, quality medical care can actually lead to an apparent increase in some diseases by virtue of better diagnosis. For example, brain tumors were found to be in excess among the work population of the Kodak Company in Rochester, New York (13). A careful analysis of this finding revealed that it was the result of improved diagnostic criteria utilized in the medical facilities of Rochester, compared to those typically utilized by the general population.

One noticeable selection factor in study populations is the finding of increased risks of mortality among individuals employed for short periods of time (14, 15). The personal factors affecting health associated with such transient populations may adversely bias a study. In many industries, if not most, approximately half the individuals that are hired quit or are terminated within a year (16). Inclusion of such individuals in a study can give rise to spurious increases in overall SMR's. On the other hand, dose-response relationships can be improperly

reduced when groups of short term workers, with possibly greater mortality risk, comprise the "low exposure" category.

The use of improper geographical comparison rates, either from the general population or from a comparison study group, can lead to higher or lower estimated risks. Care should be taken to determine whether local, state or national rates are most applicable to the analysis of mortality or morbidity in an exposed population. Generally, local rates would be the most applicable. However, these may be unstable because of small numbers or affected by other industries in the area under consideration. (c.f. the effect of local rate on the published Bertazzi study reviewed in the PCB analysis (17).) Note that even U.S. population rates are affected to some extent by occupational exposures which may not play a role in the group under analysis. For example, past asbestos exposure has been estimated to account for approximately five percent of lung cancer among males nationwide and even more in certain geographic areas (16). This necessarily inflates the comparison rates that will be used to ascertain disease in a population unexposed to asbestos.

SURVIVOR EFFECTS

In addition to the selection factors mentioned above, important survival effects can be manifest among groups of workers followed for long periods of time, particularly among those who are at high risk of death from an occupational or other exposure. For example, a substantial decline in the relative risk of lung cancer is seen among asbestos insulation workers after 40 or more years from onset of exposure (See Figure 1) (18). Part of this decline can be attributed to the elimination, through death, of cigarette smokers from the group at risk during earlier years, with the result that the population of workers under observation contains proportionately fewer cigarette smokers than the general population to which mortality is compared. During early years of follow-up, the proportion of asbestos workers who smoke is slightly greater than that of the general population, but the heavy toll of asbestos- and cigarette-related deaths among smokers substantially reduces the number of smokers between 20 and 40 years from onset of exposure. Thus, proportionately fewer cigarette smokers are left in the study group after 40 from onset of exposure than in the general population to which the study group is compared. Similarly, survivor effects relating to the study agent could occur, particularly in high risk settings. Observation of only one segment of the duration-from-exposure spectrum, a retiree population, for example, can lead to substantial errors in estimating, or even identifying, risk.

EVALUATION OF NEGATIVE STUDIES

Negative studies, in the sense that there is no elevated risk for cancer of a particular site that achieves a 95 percent level of significance, have often been used as evidence of "no effect." This is clearly wrong. Such studies only indicate the upper limit of risk in the particular circumstances studied. However, such risk limits are valuable data.

They can be used to suggest that risk estimates from animal studies may be inappropriate or that another epidemiological study might be flawed. Thus, data from negative studies should receive the same critical appraisal as positive ones.

What is most commonly done in the analysis of a negative study is to utilize the 95% upper confidence limit (UCL) on the overall SMR of cancer at a particular site or the 95% UCL of a dose-response regression. In some cases the SMR of interest may be less than 100. In such cases, the likelihood is strong that selection factors played some role in the observed deficit. Consideration of what would be the UCL of risk from such a study might best be calculated assuming the observed risk represents an SMR of 100, rather than the lower observed value. This procedure simply treats negative studies in a way similar to what is done implicitly with marginally, albeit statically significant, positive studies. Just as it is improper to uncritically accept a 20% or 25% statistically significant increased risk in a single study, without full consideration for confounding exposures, selection factors and possible biases, so too it is improper to accept a reduced risk of similar magnitude.

SUMMARY

In summary, the HWE is present, to some extent, in most epidemiological studies. It usually does not affect substantially the results of such studies as the statistical uncertainties on measured cause specific SMR's are usually much greater than the magnitude of any HWE. The presence of a HWE or selection factors in the study population can be identified and its magnitude estimated by the use of internal control populations, by the development of dose-response relationships and by the use of carefully conducted nested case-control studies with the study cohort. Despite the presence of a possible HWE, it is important that observed deaths in epidemiological studies be compared with expected deaths calculated using general population rates. Use of only internal comparison rates for estimates of expected deaths leads to a substantial reduction in the power of a study.

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TABLE 1

SELECTION FACTORS IN COHORT STUDIES

Factors associated with hiring process

1. General health at time of hire established by physical examination
2. Personal habits at time of hire through MD or Personnel Department interview

Factors associated with continuance in work

3. Loss of job because of health related factors or illness related absenteeism
4. Availability of quality medical are through employer benefit programs

Factors associated with work related risks

5. Risk-related early mortality
6. Individual susceptibility

Use of improper comparison rates in cohort analysis

7. Alteration of general population rates by occupational factors
8. Appropriateness of rates used (national, provincial, local)

TABLE 2

SMR's FOR SELECTED CAUSES AMONG VARIOUS MT. SINAI SCHOOL OF MEDICINE STUDY POPULATIONS

Agent	Minimum Latency	Minimum Expos.	All Causes	All Cancer	Lung Cancer	Colo-rect. Cancer	Leuk Lymph.	Ref.
PCBs	10 yrs.	5 yrs.	89(188)	79(44)	98(14)	89(7)	131(6)[a]	1
Vinyl Chloride	10 yrs.	5 yrs.	93(80)[b]	142(28)[b]	55(4)[a]	91(3)	263(3)[a]	2
Styrene	10 yrs.	5 yrs.	78(83)	81(17)	117(6)	--	98(2)[a]	3
Printing Inks	15 yrs.	15 yrs.	112(1232)	119(263)	131(72)[a]	79(47)	111(18)[a]	4
Asbestos Miners	20 yrs.	20 yrs.	111(178)	134(49)	252(28)[a]	105(10)[a]	--	5
Factory Workers	20 yrs.	20 yrs.	148(199)	259(72)	321(27)[a]	217(13)[a]	--	6

() No. of deaths
[a] Suspect site of agent action
[b] Includes 9 deaths of liver hemangiosarcoma

TABLE 3

SMR's FOR SELECTED CAUSES AMONG VARIOUS POPULATIONS EXPOSED TO RADIATION

Author	Minimum Latency/Exp.	All Causes	All Cancer	Lung Cancer	Colo-rect. Cancer	Leuk Lymph.	Refs.
Hadjimichael et al.	6 mo.	83(167)	88(40)	95(14)	78(10)	82(4)[a]	7
Checkoway et al.	1 mo.	73(966)	78(194)	75(59)	48(14)	97(28)[a]	8
Cragle et al.	3 mo.	80(728)	72(130)	85(53)	75(14)	87(19)[a]	9
Beral et al.	0	78(2856)	79(827)	72(274)	--	102(74)[a]	10

() No. of deaths
[a] Suspect site of agent action

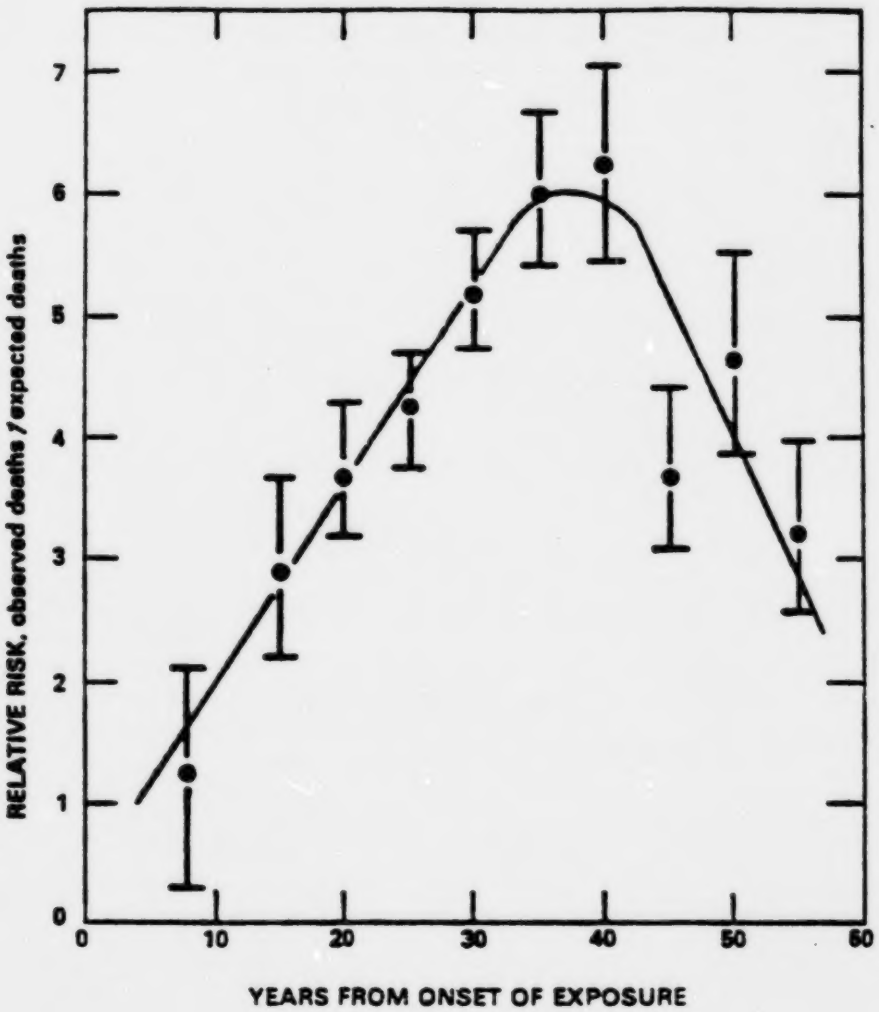

Figure 1 The relative risk of death from lung cancer among insulation workers according to time from onset of exposure

OBSERVATIONS ON POSSIBLE SOURCES, EXTENT, PERSISTENCE, CONSTANCY, AND CORRECTIONS FOR THE HEALTHY WORKER EFFECT

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ABSTRACT

The issue raised by the Healthy Worker Effect (HWE), is that the degree of risk for a specific disease or cause of death from occupational exposure could be underestimated if the mortality rate of an employed group is compared with the mortality rate of the general population. Data from the U.S. National Health interview survey show that employed are consistently healthier than not employed for all ages. A follow-up of 250,000 holders of U.S. Veteran Insurance Policies, who can be considered of equivalent health to employable individuals, shows that the HWE reduces mortality for all causes by about 25% appears to affect all disease categories and appears to persist throughout life. Examples of possible misleading results and incorrect conclusions are presented. A method of correcting estimated risks and computing confidence intervals for the corrected estimates is presented and examples from the literature are analyzed.

INTRODUCTION

Investigations of possible occupational hazards encounter the so-called Healthy Worker Effect (HWE) as a recurring phenomenon. In a narrow sense, the HWE refers to the frequent observation that the mortality or morbidity of a cohort followed in an occupational health study is less than that of the general population. In a wider sense, the issue is that individuals entering the labour force are in reasonably good health. Also, they must remain in reasonably good health to retain employment. As a consequence, mortality or morbidity rates of occupational groups are generally lower than those of the general population because, in comparing the mortality or the morbidity of a particular occupational group with that of the general population, one compares individuals who are sufficiently healthy to hold employment (the Occupational Group) with a population that includes many individuals who do not seek employment for reasons of health. (Ogle, 1985; Fox, 1976; McMichael, 1976; Ott, 1976; Vinni, 1980; Wong, 1982; Sterling, 1985, 1986; Monson, 1986)

The issue, then, is that if a working population is already healthier than the general population, the degree of risk for a specific disease or cause of death from occupational exposure could be underestimated. Consequently, as Monson pointed out, "Uncertainty about the strength and extent of the HWE has led to uncertainty in interpreting data from studies in which the mortality rate of an employed group is compared with the mortality rate of the general population." (Monson, 1986; page 425)

In this discussion we shall briefly summarize evidence for the source, extent, persistence, constancy of the HWE, give examples of how the HWE may lead to misleading conclusions and discuss possible ways of correcting for the HWE.

THE DIFFERENCE IN HEALTH BETWEEN EMPLOYED AND UNEMPLOYED PERSONS

One source of evidence that the health status of individuals who are employed is different from that of those who are not comes from a study of the large probability sample of the U.S. population, the National Health Interview Survey (NHIS). Observations were based on interviews with 142,281 men and 157,538 women during combined survey years 1969 to 1974 (Sterling, 1985). The U.S. NHIS (an ongoing health survey of approximately 40,000 households) includes questions on occupation and on health conditions. Among occupational categories are employed, unemployed seeking employment, and unemployed not seeking employment. Among health condition categories are various types of chronic and acute conditions and impairments. Age specific morbidity ratios were computed for a number of health conditions for males and females in different employment categories.

Figure 1 shows age specific morbidity ratios for total chronic disease for all males between the ages of 25 and 59 years. (These ages are selected because they span the years of most stable employment.) For those employed, morbidity ratios are lower than 1.0 at age 25 and decrease constantly in a linear fashion to age 59. Ratios for the total unemployed group and larger than 1.0 and increase sharply in curve linear fashion leveling off at age 40. There is a considerable difference in the way age specific ratios behave for increasing ages by type of unemployment. For those seeking employment, the morbidity ratios fluctuate between approximately 1.2 and 1.4. The ratios for those not seeking employment begin at an even higher level, and increase sharply to age 40 and only then begin to decrease. Age specific ratios for females and for other measures of morbidity (days of restricted activities, chronic respiratory illness, and impairments) are almost identical to the curves shown in Figure 1. The information in Figure 1 is briefly summarized in Table 1 which shows morbidity ratios for white males and females for ages 25 to 59 for different employment categories.

The unemployed for the years of the study make up 8% of white male population, and those not seeking employment make up 6% (or 75% of the unemployed), there is a considerable number of individuals in the

general population who are not employed and who have higher chronic disease rates than those who are employed. The analysis of the NHIS data then demonstrates that there is considerably more chronic disease among the unemployed than the employed.

THE EXTENT, PERSISTENCE AND CONSTANCY OF THE HWE

Three questions need to be answered to assess the major influence of the HWE.

1. What is the magnitude of the HWE?

2. Does the magnitude of the HWE change with age?

3. How does the HWE differ for different disease categories?

It turns out that there is an extremely suitable source of data on which to base answers on the magnitude, persistence, and constancy of the HWE. Those data were collected as part of a follow-up of approximately 250,000 U.S. veterans of the armed services who held active government life insurance policies in 1953 and who had served between 1917 and 1940. The data are ideal to compare the mortality of the general population to that of a population which consists of persons who could only be included if they were healthy at the age when young adults usually seek employment. Persons who qualify to serve in the armed forces, in a way, are certified as being healthy at the time of their induction. Thus, they constitute a population of persons for whom there is a reasonable expectation that they are employable. Since the study population consists of paying holders of a special insurance policy, the chances are that most participating veterans were employed. Also, few seriously disabled persons would be included, as support for service-connected disability is handled under special public laws. (The data are, however, not suitable to analyze the HWE among women or among non-whites because almost all of these U.S. veterans were white males.)

Table 2 summarizes mortality ratios standardized to the general U.S. population for all causes and for a number of specific causes. Age groups given are 35 to 54, 55 to 84, and the total age range 35 to 84.

With respect to the extent of the HWE, the mortality of healthy persons from all causes is approximately 73% of the mortality of the total population.

With respect to constancy, the HWE appears to effect all disease categories. (Some of the variations in mortality ratios are probably due to the small number of deaths in some categories. For instance, the ratio for kidney cancer is based on only 269 deaths and that for oral cancer on only 251. (Many of the five-year age groups have no deaths at all from these causes or only 1 or 2.) However, the number of deaths is sufficiently large for reliable estimates for all causes (48,664), all cancers (9,332), lung cancer (2,068), heart disease (25,325), and stroke (3,627).)

The HWE appears to be greater for respiratory and lung cancer than it is for all causes. This observation is important because it is precisely these diseases (cancer, respiratory cancer, lung cancer) that are of major interest to many occupational health studies. Cancer is also the disease to which some investigators have claimed the HWE does not apply.

With respect to the change of the HWE with time, the comparison of mortality ratios for ages 35-54 to 55-84 indicates that while there might be a slight general decrease in magnitude of HWE (i.e. a slight increase in the SMRs) with increasing age, the decrease does not appear to be large.

While the mortality data apply only to men, there is no reason to suspect that the HWE for female mortality is different from that of men.

Considering both the morbidity and mortality data, we conclude that the HWE:

1. reduces mortality of the employed by some 25% from that expected when the mortality is computed for the total population,

2. appears to affect all disease categories approximately equally, including cancer and heart disease, and

3. appears to persist for the lifetime of the individuals.

EXAMPLES OF POSSIBLE MISLEADING RESULTS

There are instances where chronic exposure to an occupational hazard may result in an increased risk of lung cancer. Yet, a lifetime follow-up that standardizes the observed mortality of an occupational group with reference to the mortality of the general population may miss such occupational hazards entirely. Table 3 shows the outcome of a study by Sterling (1962) in which some 9,000 coke oven workers were followed from 1940 to 1957. That table gives the SMRs for lung cancer, other cancer, coronary disease, all other causes and all causes, for ages 25-64, 65 and over, and 25 and over.

SMRs for lifetime follow-up (i.e. for ages 25 and up) appear to show no particular effect due to exposure to coke oven emissions. The SMR for all causes is 0.91 while those for lung cancer, other cancers and coronary disease are close to 1.0, as expected based on the general population. However, the picture is quite different when SMRs are computed for ages 65 and older. Significant increases in risk for lung and other cancers as well as coronary disease may be observed. The reason these increases in risk are not apparent for the total age range lies with the HWE for younger ages. As we now know, the increase in lung cancer risk for coke oven workers is detectable only after prolonged exposure.

Table 4 shows another example of a possible increase in lung cancer risk among chemical workers exposed to formaldehyde that appears to have been

hidden by the method used to standardize mortality. In this study, Acheson et al. (1984) standardized the mortality rates of a large cohort of chemical workers using the general population and also the population living in the same region as the workers in their sample. They report an SMR of 0.87 for all causes, of 1.02 for respiratory disease, of 0.97 for malignant tumors including lung cancer, and of 0.95 for lung cancer. Acheson et al. included sufficient information in their report for computation of a Proportional Mortality Ratio (PMR) for workers exposed to high doses, using the mortality distribution among individuals with low exposure as the standard. In their recalculation, Sterling and Arundel (1985) find that the PMR for respiratory disease and lung cancer are both significantly elevated. These results are similar to those of Wong (1983) where an SMR based on the general population failed to find a significant increase in lung cancer risk the PMR did so. While there are some disadvantages to the PMR as a measure of risk, at least it offers some control for the HWE.

CORRECTING FOR THE HEALTHY WORKER EFFECT

The two examples of misleading studies indicate that some corrections for HWE are possible. One method of correction tests for an increase in specific disease SMRs with age. Such an increase would indicate an effect of chronic exposure to a health hazard, even if the disease specific SMR does not ever exceed unity by a significant amount.

Another possible control is to standardize mortality ratios for individuals with high exposure to the mortality of individuals with low or no exposure.

Unfortunately, this last requirement often is forbidding. Effective exposure levels are difficult to measure under the best conditions and, in retrospective/prospective cohort studies, clear cut exposure differences are often impossible to determine with adequate reliability.

The PMR as a measure of risk affords some protection from the HWE. But the PMR is not suitable to determine relative risk. Besides, the PMR could miss an increase in disease specific risk following prolonged exposure (as in Sterling et al.'s 1962 study of coke oven workers).

Monson (1986) concludes that the HWE is a phenomenon of confounding rather than of selection bias. Selection bias occurs because of the action of an investigator. On the other hand, the HWE is a characteristic of the study population and, therefore, an example of confounding. "The confounding factor is the (unmeasured) health status of the group of employees." (page 431) The distinction between confounding and selection bias is important because it is often possible to correct for confounding if it is possible to estimate the overall confounding effect in the industrial cohort with respect to the standardizing population. The correction may be accomplished by dividing the SMR of interest (eg. for lung cancer) by a comparable SMR that is less affected by the occupational exposure in question. Several choices for the latter seem possible:

1. The observed SMR for a specific cause could be adjusted by dividing by the observed SMR for all causes within the same study.

2. The observed SMR for a specific cause could be adjusted by dividing by the observed SMR from the same study for another specific cause that is thought to be unrelated to exposure. (i.e., the SMR for lung cancer could be divided by the SMR for cardiovascular disease, accidents, or other causes.)

3. The observed SMR for a specific cause could be adjusted by dividing by the observed SMR for all causes from the large U.S. Veteran Study, i.e. by 0.73.

4. The observed SMR for specific cause could be adjusted by dividing by the SMR for that same specific cause in the U.S. Veteran's data. (i.e. Dividing an observed lung cancer SMR by 0.65.)

Table 5 explores the effect of these suggested methods of adjusting for confounding by the HWE. The studies serving as examples come from a recent search through the occupational health literature to locate investigations with sufficient information to adjust for the HWE (Sterling, 1988). Table 5 shows six such studies and the SMRs they reported for all causes and lung cancers. It also shows the results of adjusting the observed SMR for lung cancer 1) using the SMR of all causes observed in the same study, 2) using the SMR for Cardiovascular Disease observed in the same study, 3) using the U.S. Veteran SMR of 0.73 for all causes, and 4) using the U.S. Veterans SMR of 0.65 for lung cancer.

The adjustments increase the lung cancer SMR by a relatively large amount in all instances. In case of Rockette (1983), Morgan (1981), and Hadjimichael (1983) adjusting the SMR for lung cancer using the observed SMR for all causes increases that ratio from less than 1.0 to 1.13, 1.14, and 1.12 respectively. This represents an increase of approximately 20% in estimated relative risk. Adjusting the lung cancer SMR using the U.S. Veteran study, increases the ratio by a considerably greater amount.

The other three studies by Wang (1979a, 1979b) and Stayner (1985) each reported a lung cancer SMR greater than 1.0. After adjustment, the excess risk for lung cancer varies between 200% and 300% of the original estimate (i.e. an excess risk of 34% becomes 86%, 13% becomes 38% and 15% becomes 37% after adjusting using the SMR observed for all causes).

Adjusting the SMR using Cardiovascular Disease appears to increase the relative risk estimate by a smaller amount than the other methods. However there is a possibility that the risk of Cardiovascular Disease is itself increased by the same exposure.

Which of the adjustment factors is preferred depends on the attitude of an investigator and the absolute magnitude of the investigated risk.

Certainly the most conservative adjustment procedure is to adjust the observed SMR for lung cancer using the observed SMR for all other causes in the same study (ie. all causes with lung cancer omitted). In the case of lung cancer, the true risks for workers in studies listed in Table 5 probably falls between the adjusted ratio using the observed SMR for all causes and the adjusted ratio using the U.S. Veteran's data for lung cancer.

CONFIDENCE INTERVALS

Each of our adjustments is a ratio of two SMRs. If confidence intervals are available for both numerator and denominator, a confidence interval for the ratio may be estimated as follows: (For simplicity we assume that all confidence intervals are at the same significance level, say 95%).

Let N and D be the numerator and denomerator and n and d be the upper endpoints of the corresponding 95% confidence intervals. The confidence interval of the adjusted SMR is given by (R/x, Rx) where

$$x = \exp\left[1.96\left[\left[\frac{\log \frac{n}{N}}{1.96}\right]^2 + \left[\frac{\log \frac{d}{D}}{1.96}\right]^2\right]^{\frac{1}{2}}\right]$$

and

$$R = \frac{N}{D}$$

Table 6 shows the confidence limits for the adjustment of the lung cancer SMRs using the All Causes SMR from the same study for those studies shown in Table 5 for which the necessary confidence limits were available.

In one of the four studies for which computation of the confidence interval of the adjusted SMR was possible, the adjusted value indicated a significant increase in risk, with $P \leq .05$. In the remaining studies, the adjustment value was still not significant by conventional criterion. However, the increase in risk might have reached conventional criterion of statistical significance, had the source data given in these reports used here included the SMR for all causes but with lung cancer removed. Even with that unavoidable shortcoming our exercises demonstrate that occupational health investigations can be reasonably adjusted for the HWE.

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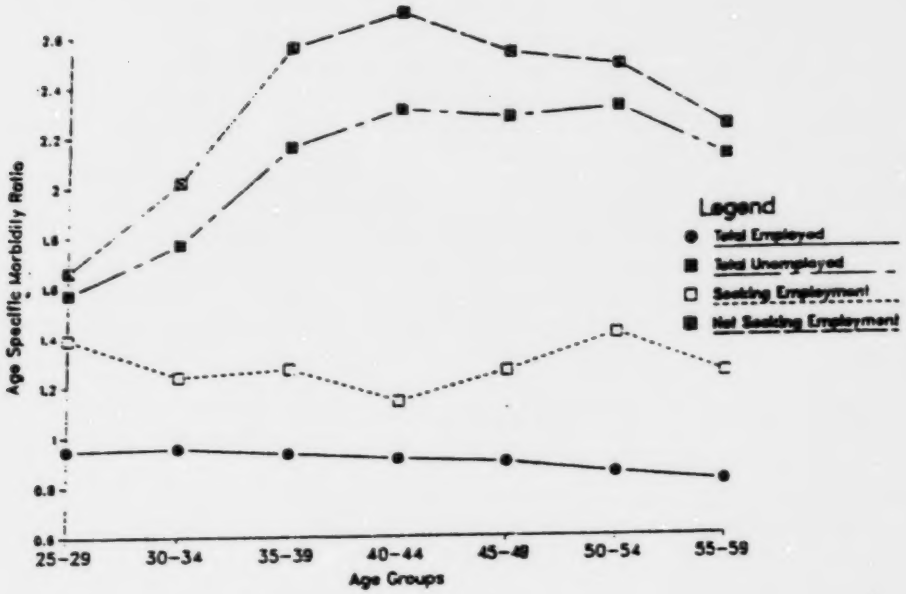
FIGURE 1

Age Specific Morbidity Ratio Of All Chronic Conditions For All Males, By Employment Group.



* From Sterling and Weinkam, 1985.

TABLE 1

Morbidity Ratios By Employment Group Standardized To Estimates For The U.S. Population (SMRs) For Males And Females In The NHIS Sample*

	Employed	Unemployed		
		Seeking Employment	Not Seeking Employment	All Unemployed
White Males	0.90	1.31	2.29	2.07
White Females	0.83	1.14	1.34	1.31

* From Sterling and Weinkam, 1985.

TABLE 2

Mortality Studies Of A Cohort Of Approximately 250,000 U.S. Veteran Life Insurance Holders Standardized To The U.S. Population (SMRs)*

Causes	Age Group		
	35–54	55–84	35–84
All Causes	0.69	0.74	0.73
All Cancer	0.68	0.77	0.76
Respiratory Cancer	0.52	0.67	0.64
Lung Cancer	0.55	0.67	0.65
Oral Cancer	0.30	0.67	0.60
Upper Digestive Tract Cancer	0.63	0.56	0.57
Colon And Rectum Cancer	0.79	0.86	0.85
Prostate Cancer	1.15	0.84	0.85
Kidney Cancer	0.93	0.97	0.97
Bladder Cancer	0.66	0.81	0.80
Heart Disease	0.67	0.75	0.74
Stroke	0.62	0.63	0.63
Accident	0.79	0.56	0.66

* From Sterling and Weinkam, 1986.

TABLE 3

Mortality Ratios Of A Cohort Of Steelworkers Standardized To The U.S. Population (SMRs) For Ages 25–64, 65 And Older, And 25 And Older*

Causes	Age Group 25–64	65 and Older	25 and Older
Lung Cancer	0.79	2.36	1.00
Other Cancers	0.77	1.84	1.04
Coronary Disease	0.90	1.27	1.00
All Other Causes	0.65	1.17	0.76
All Causes	0.78	1.34	0.91

* From Sterling, 1962.

TABLE 4

Comparison of Mortality Standardized on the General Population (Acheson et al*) and Proportional Mortality Ratios of High to Low Exposed (Sterling and Arundel**) Chemical Workers in the Manufacture of Formaldehyde Products.

Cause	Acheson et al SMR	Sterling and Arundel PMR
Respiratory Disease (not malignant)	1.02	1.46·
Malignant Tumors (including Lung Cancer)	0.97	1.13
Lung Cancer	0.95	1.54·
All Others	0.80	0.94
All	0.87	–

* Acheson et al, 1984
** Sterling and Arundel, 1985
· $p \leq .05$

TABLE 5

Observed SMRs For All Causes, All Cancers And Lung Cancer From A Number Of Recent Occupational Health Studies And Lung Cancer SMRs Adjujsted For Healthy Worker Effects Using (1) Observed SMR for All Causes, (2) Observed SMR for Cardiovascular Disease, (3) SMR For All Causes Observed Among U.S. Veterans, and (4) SMR For Lung Cancer Observed Among U.S. Veterans.

Study	N in Cohort	Observed SMRs All Causes	Observed SMRs Lung Cancers	Adjusted SMRs (1)	(2)	(3)	(4)
Rockette (1983) (Aluminum Reduction)	21,829	0.84	0.96	1.13	1.08	1.32	1.48
Morgan (1981) (Paint Coating)	16,243	0.85	0.98	1.14	1.08	1.34	1.51
Hadjimichael (1983) (Nuclear Fuels)	4,106	0.82	0.92	1.12	1.15	1.26	1.42
Wang (1979a) (Chlordane, Heptachlor)	1,403	0.72	1.34	1.86	1.61	1.84	2.06
Stayner (1985) (Fertilizer Production)	3,199	0.81	1.13	1.38	1.71	1.55	1.74
Wang (1979b) (Pesticide Applicators)	16,126	0.84	1.15	1.37	1.25	1.58	1.77

TABLE 6

Lung Cancer SMRs Adjusted By Using SMR For All Causes With Confidence Intervals For Adjusted SMR Estimated From Confidence Intervals Of The Unadjusted Values.

Study	All Causes	Unadjusted Lung Cancer	Adjusted Lung Cancer
Hadjimichael (1983)			
SMR	.82	.92	1.12
Conficence Interval	.71 to .93	.54 to 1.45	.70 to 1.80
Wang (1979a)			
SMR	.72	1.34	1.86
Confidence Interval	.59 to .86	.73 to 2.28	1.06 to 3.26
Stayner (1985)			
SMR	.82	1.13	1.38
Confidence Interval	.71 to .93	.61 to 1.92	.80 to 2.38
Wang (1979b)			
SMR	.84	1.15	1.37
Confidence Interval	.75 to .94	.77 to 1.70	.91 to 2.06

APPENDIX B

EVIDENTIARY BASE FOR THE REPORT

ON

THE HEALTHY WORKER EFFECT

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